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ORIGINAL ARTICLES.

THE USE AND ABUSE OF DIGITALIS.[1]

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Digitalis is an enduring witness of our debt to the early days of therapeutic empiricism. First brought into general use by Withering, in the latter part of the eighteenth century, as a cure for dropsy, it has become, through scientific observation at the bedside and in the laboratory, our mainstay in the treatment of cardiac disease. It is one of the few indispensable drugs. Nevertheless, skepticism as to its value is still frequently expressed. This is about as reasonable as would be distrust of the value of ligatures in surgery. Ligatures may be of poor material, and break, or being wrongly applied, they may slip, but no surgeon would, therefore, think of condemning their use. On the contrary, he would diligently look for the faults in his materials or technique.

It is high time we practitioners of internal medicine took a lesson from the great advances of modern surgery and the success of our surgical colleagues. In our more difficult field, where the sequence from cause to effect is often obscured by intermediate events, we must not make this an excuse for a less rigid criticism of our results, but rather scrutinize both apparent success and seeming failure the more closely, and resolutely improve our technique.

In this paper I purpose to discuss briefly some reasons for failure in digitalis therapy, which I have learned from personal experience, and the equally serious results of certain misconceptions, which make men withhold digitalis when it is urgently needed. The

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causes for failure in the employment of digitalis, in the order of their frequency and importance, are: (1) The use of inefficient preparations. (2) Use in unsuitable cases. (3) Improper dosage. (4) Improper methods of administration. (5) Neglect of other necessary therapeutic measures.

1. Inefficient Preparations. Few practitioners have the remotest idea how little good digitalis can be had. The majority prescribe a drug which, if good, may save life, without inquiry into its character or method of preparation, and often in a form which the least study would convince them must be inert. A surgeon, who should display similar carelessness as to the preparation of his ligatures and dressings, would speedily be brought to his senses by a suit for malpractice. We medical men must face our responsibilities in this matter of dishonesty and incompetence in the drug trade, wholesale and retail, or reap the inevitable harvest of deserved loss of confidence and of our own self-respect.

The active principles of digitalis are glucosides, which decompose readily in the presence of moisture, yielding inert or toxic products. In order that we may be sure of giving efficient digitalis, and not inactive or irritating digitalis decomposition products, the following conditions must be fulfilled: (1) The leaves must be from plants of the second year's growth, picked at the beginning of efflorescence, freed from stalks, and carefully dried. (2) The dried leaves must be kept absolutely dark and free from moisture in sealed tin or glass containers, and for not more than one year. (3) The preparation dispensed must be freshly made from these leaves in exact accordance with the method prescribed by the Dispensatory.

This obviously requires intelligence and honesty of all concerned in each step of the process. A good physician, in the present state of our knowledge, should not concern himself overmuch with pure digitalis glucosides, but should never write a prescription for digitalis without specifying that it is to be freshly made from Allen's English leaves. He should learn from personal investigation which druggists can be trusted to keep good leaves, to keep them dry and dark, and to make a fresh preparation every time it is called for. In New York I can count on a few apothecaries of this kind, and I invariably send patients to them.

The worst digitalis preparation I know is an infusion made by diluting the fluid extract, thus precipitating all of its active ingredients. This is a common practice. Another, of like kind, is an infusion made by diluting a so-called mother liquor. This was once used in a hospital with which I am connected, and digitalis came into bad repute with the staff. Other inefficient forms are the many tablets or pills containing digitalis or digitalin. The only solid form in which digitalis should be given is the freshly powdered leaf in capsule or pill. Since the dose is but one grain, there is no need for a stronger extract. The commercial digitalins are all impure

mixtures, made, as a rule, from digitalis seeds, and should only be tolerated where very mild effects are desired over a long period of time.

The use of combinations of heart tonics, usually with nitroglycerin, now sold in tablet form, is one of the most deplorable developments in therapeutics today. The practitioner, who allows himself to give powerful drugs in this way, fails to learn the action of any one of them. If he thinks at all, he becomes a skeptic; otherwise, he remains little more than the agent of some manufacturing pharmacist.

The fluid extract of digitalis, if it really represents the quantity of drug used in its preparation—and this is seriously questioned by Kobert, who claims the digitoxin is lost by precipitation—is far too strong to permit of easy regulation of dosage. I have never happened to see satisfactory results from it, and I do not favor its use.

There remain two official preparations, the infusion and the tincture, besides the powdered leaves, which, under the conditions named above, may be considered trustworthy. The choice of one of these must be largely a personal matter. One should learn how to give a single preparation and regulate its dosage under various conditions. My personal experience leads me, for most purposes, to favor the infusion, chiefly because one can be reasonably sure of having it freshly made if so specified. In case after case supposed to have been treated with digitalis without benefit, I have seen prompt results follow its use. Two cases, out of many I might adduce, should suffice for illustration.

Case I.—A retired merchant, aged fifty-one years, consulted Dr. E. G. Janeway October 3, 1907. He had a history of two severe attacks of acute rheumatism. In July, 1907, he developed dyspnœa; later, albuminuria and swelling of the legs; and a few nights ago, orthopnœa. He was slightly cyanotic, with large jugular veins and systolic venous pulse. His heart was greatly dilated, with harsh mitral systolic murmur; pulse was irregular, 120 per minute; arteries small and soft; arterial pressure, 135 mm. systolic, 100 mm. diastolic. Lungs showed congestion at bases. Liver pulsated markedly, and the edge was four inches below the costal margin. Legs showed some œdema. Urine 1022, with a trace of albumin and fine granular casts. He weighed 171¼ pounds. For some time he had been given digalen, of late taking 6 minims every four hours. He was put on infusion of digitalis, 2 drams every four hours. After a few days his urine began to increase, and October 9 he passed 120 ounces. He then weighed 161¾ pounds; œdema was gone, liver smaller, heart area decidedly diminished (hydropericardium?), and pulse only 88. On November 7 he was free from dyspnœa, weighed 156½ pounds, pulse rate was 75, and arterial pressure 120 mm. systolic, 80 mm. diastolic. This good condition has continued.

CASE II.—A man, aged sixty-one years, with chronic nephritis and chronic bronchitis, had suffered from recurring attacks of nocturnal dyspnœa, with bloody expectoration for six years. During the summer of 1906 he developed swelling of the legs, and had several attacks of intense pulmonary œdema. In October his heart was considerably larger than in the previous May, with gallop-rhythm; and the systolic pressure, which had been 190 mm., was 170 mm. His liver was much congested and legs very œdematous, with one bedsore. There was constant dyspnœa and marked cyanosis. He had taken infusion of digitalis in Saratoga for weeks without benefit, and never slept a night without half a grain of morphine.

In spite of the apparently hopeless outlook, he was put on infusion of digitalis from a reliable pharmacy. In three days diuresis set in, and the dyspnœa left him, so that morphine was stopped entirely. In a week all œdema was absorbed. A month later he was free from dyspnœa and cyanosis, the liver was normal in size, gallop-rhythm scarcely evident, and systolic pressure 195 mm. The improvement was maintained for three months.

For hypodermic injection the tincture has been most commonly employed, but it is unfortunately irritating, and often causes abscesses or large hemorrhagic areas. Much labor has been spent in the endeavor to produce an efficient but non-irritating solution of digitalis. Two recent preparations, digalen and digitalone, are said to possess both virtues. Digalen has found great favor in Germany. I cannot say that in my hands it has proved less irritating or more efficient than the tincture, and many of my colleagues have had a similar experience. Digitalone seems to me decidedly less painful and fairly active; but there is as yet no ideal form for injection, and a good tincture is, perhaps, most certain in its action. Theoretically, strophanthus or strophanthin should be employed in preference to digitalis for rapid action, but I have not sufficient clinical experience to speak clearly on this point.

2. USE IN UNSUITABLE CASES. The physician who gives digitalis to slow the heart in a paroxysm of tachycardia or in fever, to produce diuresis in acute nephritis, or to remove an inflammatory pleural effusion, is foredoomed to failure; yet all of these are attempted, and faith in digitalis for its rightful uses is lost in consequence.

The results of bedside experiment years ago made clear the indications for employing digitalis, but pharmacological studies have given us a much better insight into the reasons for these indications. In particular, the newer heart physiology, which we owe largely to Gaskell and to Engelmann, has illuminated many dark corners of the subject. We now think of the heart as an automatic organ, its muscle fibers endowed with five distinct functions: the power of originating rhythmic stimuli, conductivity for these stimuli, irrita-

bility to them, contractility, and tonicity. These functions are not evenly distributed throughout the whole heart. Normally, the rhythm originates in the auricles at the mouths of the great veins. The conducting muscular system can be traced anatomically, and, between auricles and ventricles, runs as a small bundle in the septum. The large muscular rings surrounding the mitral and tricuspid orifices are especially endowed with tone. These physiological facts have, in turn, pointed the way to the solution of many hitherto obscure pathological problems. Mitral stenosis so frequently produces irregularity of rhythm because of its tendency mechanically to damage the auricle. Stokes-Adams syndrome is now clearly the result of a lesion of the conducting bundle of His. Relative mitral and tricuspid regurgitations mean loss of tonus in the ring muscles. But, though the neurogenic theory of the heart's activity has been so generally abandoned, we must not lose sight of the great fact of nervous control. Through vagus and accelerator nerves the heart's automatic functions may be depressed or augmented, and its work coördinated to the needs of the whole organism.

Furthermore, the functions of the heart are influenced by its blood supply through the coronary vessels, by the variations in intraventricular pressure dependent on changes in arterial pressure or in the volume of blood discharged by the great veins, and by chemical alterations in the blood itself. Drugs may affect the heart in any of these ways. The digitalis series, though much remains obscure, clearly exert a direct chemical effect on the heart muscle itself, and indirect effects by vagus stimulation and vasoconstriction.

The direct action of digitalis is to increase contractility, tone, and irritability. In therapeutic doses, heightened tone and more complete ventricular emptying are evident even in the normal heart. When tone has suffered, as in dilatation, and systolic emptying is less efficient than normal, this action is still more pronounced. Loss of tone and diminution in systolic output are the cardinal indications for the use of digitalis.

Through stimulation of the vagus centre, digitalis acts to slow the heart. Unfortunately, such inhibitory action depresses tone as well as rate, and for this reason it is not a good remedy for tachycardia when no ventricular insufficiency exists. If pathological loss of tone is present, then the direct effect of digitalis on the heart muscle seems far to outweigh any indirect loss of tone through vagus influences, and slower rate brings increased efficiency. This, in turn, means improved coronary circulation and better nutrition of the heart muscle. For rapid heart action, therefore, one should use digitalis only when there is also some insufficiency of the ventricles.

Digitalis stimulates the vasomotor centre and causes more or less pronounced general vasoconstriction. This, together with improved ventricular efficiency, tends to increase the amount of blood in the arteries and diminish that in the veins. It is, therefore, the

ideal drug to combat general venous stasis. There has been a widespread fear of this vasoconstrictor action in conditions of heart weakness associated with high blood pressure, which has led many to withhold digitalis whenever hypertension is present. Strophanthus has been urged as having less general action on the arterioles. However this may be in theory, I have yet to see the strophanthus which can compare with a good infusion of digitalis in overcoming passive venous congestion and œdema, whatever the primary cause of the failing ventricle. Blood pressure observations have shown clearly that, when the heart becomes insufficient in valvular disease, arterial pressure frequently rises, and ordinarily does not fall appreciably until death approaches. Digitalis may produce a functional cure with rising, falling, or stationary blood pressure. In addition, my personal records show plainly that cardiac failure supervening on prolonged hypertension is more frequently accompanied by a pronounced fall in pressure than under any other conditions. Experience, not *a priori* reasoning, has also taught me that these cases react to digitalis surprisingly well, and that a rising blood pressure usually accompanies improvement.

Case II, already quoted, and Chart I show this clearly. Should such cases also receive vasodilators? I confess I do not know, and I am more afraid of these much-abused remedies in chronic nephritis than I am of digitalis. We must keep in mind the probable compensatory nature of much of the high tension of Bright's disease, and aim to interfere only when it can be held clearly responsible for danger. Anginal attacks, œdema of the lungs, or severe paroxysmal dyspnœa demand prompt relief of all extra strain on the heart. Gradual cardiac insufficiency, however, with falling pressure, does not seem to me at all a clear indication for vasodilators, and they should be given with careful control of their effects on arterial pressure and general capillary circulation.

Controversy has also centred around the use of digitalis in aortic insufficiency. To my mind the indications here are quite the same. We aim to correct function, not structural defects. Is there loss of tone and diminishing systolic output, with scanty urine, congested liver, and dropsy? Then give digitalis. When these phenomena appear in aortic disease, relative mitral incompetency frequently shows itself, and therapeutically and physiologically the problem differs little from primary mitral regurgitation. On the other hand, if the symptoms are merely orthopnœa or paroxysmal dyspnœa, or anginoid pain, then digitalis has no place. We should get away from anatomical categories in our medical treatment. Restitution of tissues we must leave to the inherent forces of the cells. Surgery alone attempts to repair structural damage. Medical therapeutics seeks restoration of normal function and must think in physiological terms. Nowhere is this more important than in dealing with the diseased heart, of which a correct anatomical diag-

nosis is so frequently possible as to tempt one to be satisfied with it alone.

One great advantage of the surgeon in estimating his successes has always impressed me in this connection. In all his statistics, inoperable cases are carefully eliminated from the calculation of results. Now, we medical men have our inoperable cases, too; more of them than the surgeon. We must endeavor to restore function, even when anatomical change has progressed to a degree incompatible with life. This is our duty. But, when we come to query the value of this or that method of treatment, we are justified in

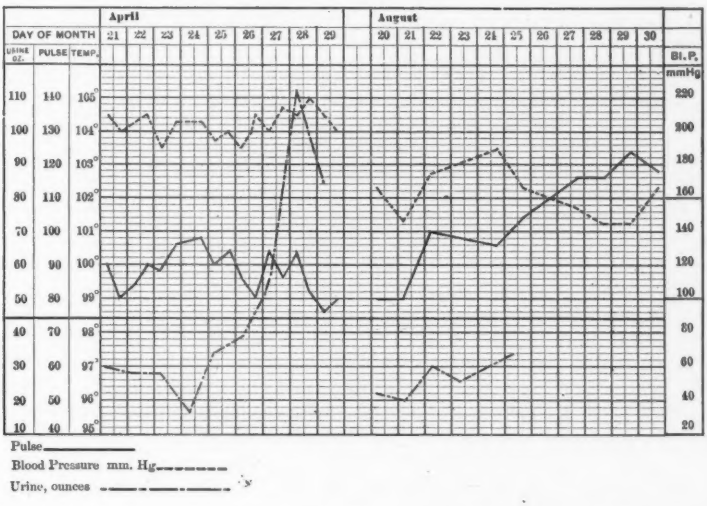

CHART I.—From man, about fifty years of age, with chronic nephritis and mitral insufficiency. April 21 to 29, prompt response to digitalis, with diuresis and rising blood-pressure and absorption of œdema. August 20 to 30, terminal fall in blood-pressure and rising pulse-rate uninfluenced by treatment. Died August 30, in the City Hospital.

attempting to separate such cases as well as may be. If, for example, autopsy shows an extreme mitral narrowing, we must not blame digitalis for failing to save the patient. This postmortem elimination of medically inoperable cases seems to me needful, if we are to escape a pessimism which will cut short our usefulness as practitioners.

3. IMPROPER DOSAGE. The question of dosage is inseparable from the question of an efficient preparation. Text-books give half an ounce as the usual dose of digitalis infusion. I seldom need to use more than two drams of a good infusion, and larger doses of a poor preparation are mainly successful in deranging digestion.

How, then, when we are dealing with such variable quantities, shall we set up any guide to dosage?

The answer is simple. The only guide is the therapeutic result. This means a clear-cut picture of the indications for the drug in the particular case, close observation of its effects, and knowledge of its earliest toxic manifestations. Digitalis should never be pushed for more than a few days without careful records of heart as well as pulse rate, and of the amounts of fluid taken and urine passed each twenty-four hours. In cases of hypertension, blood pressure should also be recorded. Daily weighings are of great value in

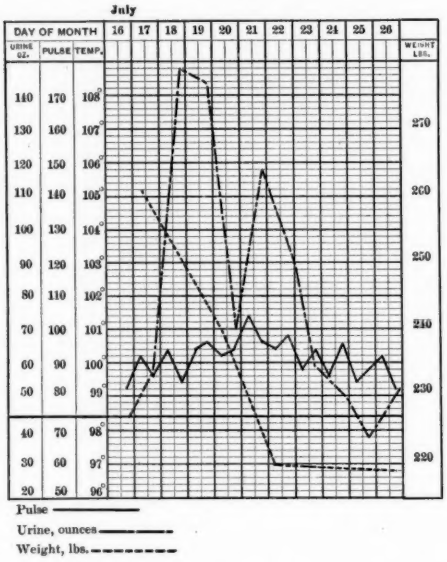

CHART II.—Rapid diuresis and loss of weight from absorption of general œdema and ascites, in a man aged thirty-eight years, suffering from chronic nephritis and dilated heart. St. Luke's Hospital.

watching subsidence of œdema. Careful observation of the extremities, the serous cavities, the size of the liver, and the changes in size, sounds, and rhythm of the heart should be an established habit. In hospitals, graphic records are an immense help (Charts I and II). With these precautions, the dosage of an infusion may be increased from two drams to perhaps half an ounce, and of the tincture from ten minims to twenty minims every four hours. I do not believe the greater quantities should be exceeded, and they should rarely be necessary. Trial of digitalis procured from a different apothecary will be likely to succeed better. Of course

forty-eight hours must elapse before the effects can be looked for.

Any marked decrease in urine is a danger signal not to be neglected, for, with diminished excretion of the drug, cumulative effects may supervene. Marked slowness and irregularity of the heart evidence the second stage of digitalis poisoning, with excessive vagus action. This stage may be wanting, however, and increasing rate, with irregularity, marks the onset of the third stage, due to excessive irritability of the heart muscle. Practically it is often difficult to be sure whether this condition, coming in a heart previously rapid and irregular, is due to too much or too little of the drug. Only careful record of the preceding events, and of the amounts of digitalis given, will permit of certain conclusions.

For minor grades of cardiac insufficiency, the continued use of small doses for weeks or months is often of advantage. These should be given at long intervals, every twelve or twenty-four hours, since digitalis is absorbed and excreted slowly.

4. Improper Methods of Administration. One of the commonest errors in judgment in digitalis therapy is persistence in administering it by the mouth, when frequent vomiting shows how little hope there is for absorption from the stomach. An equally serious error, under similar circumstances, is to withhold it altogether. Two other paths of absorption are readily available; the rectum, and the subcutaneous tissues. The rectum should always be given a trial when the stomach is intolerant and rapid action is not demanded. Half an ounce of infusion, three times a day, will give about as prompt results as by mouth.

Urgent symptoms and extreme passive congestion of the abdominal viscera are clear indications for hypodermic administration. Special cleanliness should be insisted on, because of the irritant nature of the solutions. Digalen has the merit of availability for intravenous use, and this may be recommended in desperate cases as a temporary expedient. The effect is naturally much more rapid. Intramuscular injection may also be tried.

The old-fashioned digitalis poultice, though some of its virtues were unquestionably absorbed, seems too uncertain for digitalis effect, and too costly as a poultice, to survive.

5. Neglect of Other Necessary Therapeutic Measures. To suggest that more than digitalis is needed in most heart cases seems an almost unnecessary commonplace. Not quite unnecessary, unfortunately, my experience has taught me. First in the list of adjuvant measures stands rest. This is least likely to be forgotten. Sleep is more often lost sight of. A few nights, robbed of their sufferings by morphine, may turn the scale and allow our other measures to work a cure. I remember one striking mitral case I was called to see, in which digitalis had been tried ineffectually for months and hope had been abandoned. Œdema was extreme.

For several weeks continued sleep had been out of the question. Two night's rest with morphine and forty-eight hours of tincture of digitalis hypodermically established diuresis and secured entire comfort. Infusion by the mouth completed the cure. The patient returned a few months later to her active duties as head of a very useful charitable society.

Restriction of the fluid intake, so essential in dropsical patients, is often forgotten, and the waterlogged sufferers thoughtlessly put on a milk diet. As an adjuvant treatment, the dry diet stands high. In like manner, free purgation will help relieve the secondary portal congestion, which causes much of the digestive disturbance in circulatory disease.

When anemia is marked, iron is essential, for anemia itself causes loss of tone of the heart muscle. In a different category come the vasodilating drugs, which must be given with digitalis to counteract its arterial constriction in certain cases of hypertension. I have already discussed this.

Finally, one of the more newly heralded therapeutic methods, new in name and conscious existence, but as old as the practice of the healing art, should be ever in mind at the bedside of the anxious victim of heart disease. I mean psychotherapy. Cheerfulness, courage, hope—these we should dipense in full measure at every visit, and they must come from the treasury of our own minds. If we would possess them, we must gain that confidence in the measures we employ which comes of thorough knowledge, and of the memory of wonderful results which have followed our intelligent use of digitalis in similar cases.

THE CLINICAL STUDY OF HEART CASES.[1]

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In the time allotted to me in the program of the evening it is obviously quite impossible to cover in any systematic way the subject of the clinical study of the heart. I cannot hope, and shall not attempt, to do more than touch upon a few isolated points which seem to me especially worthy of emphasis and refer briefly to one or two of the newer methods of clinical investigation.

It goes without saying that the clinical study of the heart is something vastly different from the mere physical examination of that organ. This latter, indeed, may be a relatively unimportant part of

[1] Read by invitation at a meeting of the Section on General Medicine of the College of Physicians of Philadelphia, January 13, 1908.

the study. Cases are not rare in which the physical exploration of the heart itself yields comparatively negative results, and yet the existence of serious organic mischief there is made plainly evident, either by the subjective symptoms or by some such obvious changes in other parts of the body as swelling and tenderness of the liver, marked pulsation in the veins of the neck, or œdematous swelling of the ankles. On the other hand, the presence of a heart murmur may have little or no practical significance if there are lacking all other evidences of cardiac and circulatory disturbance.

I trust I may be forgiven if, first of all, I take time to call attention to the urgent need of a careful inquiry not only into the existing subjective symptoms, but into the earlier history of the patient as well. Often a proper interpretation of the physical signs can be made only with the aid of such knowledge. It is obvious, for example, that a systolic murmur over the pulmonic area occurring in a child who has been more or less cyanotic since its birth has a very different significance from a similar one heard in a young woman with the history and symptoms of chlorosis, or from one found in a laborer, aged forty-five years, with a history of syphilis and of such symptoms as severe throacic pain and a hard, ringing cough.

Physical Examination of the Heart. Although in theory we are probably all agreed as to the necessity of employing, in the study of the heart, all the usual methods of physical examination—inspection, palpation, percussion, and auscultation—in practice I fear we are, many of us, prone to devote most of our time and thought to auscultation alone. This I am sure is a grave mistake. If, as Voltaire has said, speech is often a device for the concealment of one's thoughts, it is an equally true paradox that auscultation is sometimes a means of confusing and concealing a diagnosis. To make it of value it must have the support of the other methods of examination, and I do not hesitate to express my belief that the intelligent use of the combined methods of inspection and palpation will, in general, supply us with more useful information concerning heart conditions than will auscultation. The commonest sin of omission in the study of heart cases is, it seems to me, the neglect of these two most valuable methods of investigation.

The Venous Pulse. One of the important recent advances in the clinical study of the heart owes most of its stimulus to the work and writings of James Mackenzie[2] of Burnley, England, whose study of the venous pulse has done so much to make clear the significance of many of these vein movements in the neck and to direct attention to their clinical value as an index of the workings of the right auricle and ventricle. Mackenzie has also devised a simple instrument, the clinical polygraph, by means of which graphic

[2] The Study of the Pulse, London, 1902.

tracings of these venous pulsations in the neck and liver are recorded in connection with ordinary sphygmographic tracings of the radial pulse—the two records running side by side on the same strip of paper.[3] By comparison with the tracing of the arterial pulse the complicated movements of the venous tracing may thus be accurately timed and rendered intelligible. Such graphic records are essential to the satisfactory study of the venous, pulse since many of the movements are too small and rapid to admit of their being accurately noted by the unaided eye or finger.

Mackenzie has shown, among many other interesting things, that the so-called negative or normal, presystolic pulse in the veins of the neck is neither negative nor normal, but is a true regurgitant pulse from the auricle, and that, moreover, it is usually associated with a more or less distinct systolic wave indicative, he believes, of some slight tricuspid incompetency.

This method of studying the disturbances of the right side of the heart, by means of the clinical polygraph, is simple enough to permit it to be used in the ordinary clinical examinations at the bedside or in the consulting room and deserves a much more general use than it has thus far had in this country.

ORTHODIAGRAPHY. It will be generally admitted, I think, that the usefulness of the *x*-rays in the study of the heart has been much less than might naturally have been expected. The chief reason for this is to be found in the magnification and distortion of the outlines of the heart which are given to the shadow projected upon the photographic plate or fluoroscopic screen by the divergence of the rays as they come from their single point of origin at the anode. Since the degree of magnification depends not only upon the distance of the heart from the anode, but also upon the distance of the heart from the plate or screen, and since these two distances must vary with the depth of the chest, it has not been possible to formulate a general rule by which the error could be measured and allowed for. Thus far the most successful plan for obviating this difficulty has come from Moritz[4] in the method to which he has given the name of orthodiagraphy. The method has attracted wide interest in Germany, and seems to have become firmly established as much the most accurate means yet discovered for determining the size and contour of the heart. Time will not permit a detailed description of the apparatus, but its essential feature is a device for utilizing only the central rays coming from an ordinary Crookes' tube—those which fall perpendicularly upon the fluoroscopic screen. By moving the tube from place to place and by using only the perpendicular rays various points upon the circumference of the heart are determined in succession and marked upon the screen or chest

[3] More recently McKenzie has devised an excellent portable ink-writing polygraph.

[4] Münch. med. Woch., 1900, xlvii, 992; 1902, xlix, 1; Deut. Archiv f. klin. Med., lxxxi, 1, and lxxxii, 1.

wall. By the joining of these points an outline is obtained which represents very closely the true projection of the heart. As the method requires a somewhat elaborate apparatus as well as the services of a trained operator its use is likely to be restricted to such hospitals and other institutions as have a well-equipped radiographic department, but as it is at present the most accurate method known for determining the size of the heart its development marks a distinct advance in the study of that organ.

By means of it Moritz, Dietlen,[5] and others have made extensive statistical studies of the size, position, and form of the heart under both normal and pathological conditions. Among the many interesting facts thus elicited may be mentioned:

1. That with the change from the recumbent to the erect position there is a distinct sinking of the heart of from 2 to 4.5 cm., corresponding to the lower position of the diaphragm and liver, and that with this the heart assumes a more nearly vertical position, while the width of its shadow is considerably lessened.

2. That in old age there is regularly a lower level of the diaphragm and a correspondingly lower position of the heart, but in this case the organ, instead of having a more vertical position than usual, occupies one more nearly transverse. The explanation of this is probably to be found in the relaxation of the attachments of the great vessels by which the heart is held in position.

3. That in women the position of the heart is on the average an intercostal space higher than in men; and

4. That in asthma and emphysema there is a marked sinking of the diaphragm and heart, and that to this fact, even more than to the overlapping of the heart by the voluminous lungs, is to be ascribed the great diminution of the heart sounds in the second intercostal space and the low position of the upper border of cardiac dulness.

Percussion of the Heart. The development of the method of orthodiagraphy, so far from tending to cause the abandonment of percussion as a means of determining the outlines of the heart, has seemed indeed to increase the interest in it, for in the former method we now have a trustworthy gauge by which the accuracy of the various methods of percussion may be measured and their clinical value estimated. Some idea of the interest which has been aroused in the subject may be had from the fact that within the last two years no less than eighteen important papers and monographs upon the various aspects of cardiac percussion have come from Germany alone.[6] Probably the most important recent work on the subject is that of Moritz[7] and his pupil Dietlen.[8] Using orthodiagraphy to

[5] Deut. Archiv f. klin. Med., lxxxviii, 55.

[6] A full bibliography of the subject of heart percussion will be found in the monograph of Aravantinos, Die Percussion in der Bestimmung der Herzgrenzen, Berlin, 1907.

[7] Verhandl. d. XIX Congress. f. inn. Med., 1901, p. 524.

[8] See Moritz, Methoden der Herzuntersuchung, Deutsche Klinik, Band iv, Abt. ii, Nr. 15.

control their work they have tested the various methods of percussion with a view to determining the one which gives results most nearly in accord with their orthodiagraphic findings. Their conclusions are, briefly, as follows:

In order to obtain all the information possible it is necessary to outline both the relative and the absolute dulness. Contrary to the belief of many, it is possible by means of the relative cardiac dulness to obtain upon the chest wall a close approximation of the true projection figure of the heart. In determining the right border of relative dulness percussion should be made during forced expiration and with long and fairly heavy strokes, the pleximeter finger being pressed firmly against the chest. In determining the upper and left border of the heart the examination should be made during quiet breathing rather than forced expiration as the position of these borders is considerably changed by active respiratory movements.

In outlining the upper border and the upper part of the left border the percussion strokes should be especially heavy, as the layer of lung covering the heart is thickest at this point, and it is easy to make the error of placing the upper border too low. On the other hand, in mapping out the lower part of the left border, a common error is to place it too far to the left. This is most likely to occur in chests in which the lateral backward curve is marked and begins close to the sternum, and in cases in which the heart is much enlarged to the left. Under such circumstances heavy percussion will tend to bring out the dulness of the lateral aspect of the heart rather than that of its frontal surface only. For this reason percussion at this point should be light rather than heavy.

Orthodiagraphic studies have shown that, under pathological conditions, the apex beat is not a safe index either of the left border of the heart or of its lower border. Sometimes the beat occurs somewhat within the limits of the true border; sometimes, on the contrary, the shock transmitted to the chest wall may extend well beyond the left border. The lower border of the apex is to be found at a considerable distance below the position of the apex beat.

In order to determine accurately the length of the heart it is important to outline carefully both the left and the lower border of the apical portion. This, Moritz believes, can be done correctly in a majority of the cases, although it is, he admits, the least reliable part of cardiac percussion. The measurements of chief importance are three: (1) The long diameter; that is, the distance from the true apex to the point of junction between the upper right border of heart dulness and that of the great vessels (auricle-cava angle). In adults this measurement averages from 13 to 14 cm. according to sex, height, and weight. (2) The distance from the midsternal line to the point of dulness farthest to the right (average 3.5 to 4.5 cm.). (3) The distance from the midsternal line to the point of dulness farthest to the left (average 7.5 to 8.5 cm.).

In a large series of cases Dietlen determined these three measurements by the method of percussion just described, and compared them with the dimensions obtained in each case by subsequent orthodiagraphic examination. Counting errors of 0.5 cm. or less as negligible, his results are as follows:

In 135 males of from fifteen to seventy years:

	Per cent.
Distance to right, correct in	87
Distance to left, correct in	72
Both measurements, correct in	64
Long diameter, correct in	81
All three measurements, correct in	52

In 71 females of fifteen to sixty-one years:

	Per cent.
Distance to right, correct in	86
Distance to left, correct in	69
Both measurements, correct in	60
Long diameter, correct in	62
All three measurements, correct in	41

In 25 children of from three to fourteen years:

	Per cent.
Distance to right, correct in	100
Distance to left, correct in	96
Both measurements, correct in	96
Long diameter, correct in	92
All three measurements, correct in	88

It will be seen that his results were extremely good in children, whose thin and flexible chest walls furnish especially favorable conditions, and were least accurate in women. In this latter class it was the presence of large, fat breasts that made percussion difficult and inaccurate, especially in outlining the left border and the apical region.

My own experience with the above method of outlining the heart, while still too limited to permit me to pass judgment upon it, is yet sufficient to convince me that it is a more satisfactory method than any other that I have used, and that if pains are taken in carrying out the details it will, in a majority of cases, furnish a reasonably accurate projection of the circumference of the heart.

Concerning Goldscheider's[9] method of outlining the heart by extremely light percussion opinions differ. It has received some enthusiastic support, but the weight of evidence, thus far, seems opposed to it.[10] It is difficult, certainly, to find justification for it upon theoretical grounds.

As to the value of the absolute cardiac dulness a word should be said. Although there is very general agreement as to its normal limits and as to the need of using very light percussion in eliciting it, there still exists some difference of opinion concerning its usefulness.

[9] Ueber Herzpercussion, Deut. med. Woch., 1905, xxxi, 333, 382.

[10] See discussion by Aravantinos, loc. cit.

Moritz insists that it should always be determined, since it often furnishes information which the relative dulness does not. He believes its increase to be conditioned especially upon dilatation of the right ventricle, and he points out that the area of absolute dulness may be considerable enlarged when there is little or no change in the limits of relative dulness.

AUSCULTATION OF THE HEART. Concerning auscultation of the heart, there is time to touch upon only two or three points. Mackenzie[11] has made the interesting observation that in cases of mitral stenosis with secondary tricuspid insufficiency, when the venous pulse is of the systolic or ventricular type a presystolic murmur is never heard. The mitral murmur either occurs in the early part of the diastole or is absent altogether. In order that tricuspid insufficiency may produce a systolic venous pulse, it is obviously necessary that the right auricle be full of blood at the time when normally it is empty—that is, at the beginning of ventricular systole—for otherwise the blood regurgitated from the ventricle would be taken up by the empty auricle and its wave would not be transmitted to the veins. Mackenzie argues, therefore, that when there is a systolic venous pulse the right auricle must be so overdistended as to be incapable of effective contraction, or, in other words, that it is, for the time being paralyzed. He suggests that in the cases of mitral stenosis with tricuspid insufficiency and a systolic venous pulse, the constant absence of a presystolic mitral murmur can best be explained by supposing that under such circumstances there is paralysis of the left auricle as well as of the right. This theory finds some support in the recent recognition by physiologists of the dependence of the left auricle for its rhythmic impulse upon the integrity of the right auricle.[12]

The frequency with which, in cases of obvious tricuspid insufficiency, the usual systolic murmur at the base of the sternum is lacking has often been noted. I have convinced myself that in some of these cases the murmur is placed much higher than usual, and may be clearly audible in the second and third left spaces close to the sternum when it is absent altogether from the location commonly ascribed to it.

Lastly, reference may here be made to a point to which I have recently called attention,[13] namely, that the diastolic murmur of aortic insufficiency seems often to possess a quality which lends itself but poorly to transmission through the stethoscope, and that not infrequently a faint diastolic murmur may be heard with the naked ear when it is quite inaudible through the stethoscope.

[11] Loc. cit.; also Quarterly Journal of Medicine, October, 1907.
[12] Erlanger and Blackman, Amer. Jour. Phys., 1907, xix, 125.
[13] New York Med. Jour., July 13, 1907.

IRREGULARITIES OF THE HEART RESULTING FROM DISTURBED CONDUCTIVITY.[1]

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Since the publication, in 1883, of Gaskell's experiments upon the heart of the tortoise,[2] the view has prevailed in physiology that the *primum movens* of the cold-blooded heart is located in or near the mouths of the great veins. Here the property of automatic rhythmicity is most highly developed, and here, therefore, arise the impulses which set the pace of the whole heart. These impulses arise at regular intervals near the mouths of the great veins and sweep over the heart, causing sinus venosus, auricles, ventricle, and bulbus arteriosus to contract successively in the order here given.

The presentation by Gaskell of an abundance of evidence proved these fundamental facts. For our purpose it will suffice, however, to refer to but one phase of this work, namely, that dealing with the blocking of the impulse on its way through the heart. This may be accomplished, as was shown by Gaskell, in one of two ways: (1) The impulse may be blocked gradually by cutting across the heart transversely at any level. When this is done carefully and gradually a stage is eventually reached in which that part of the heart located below the cut (this may be conveniently termed the distal heart) will beat perceptibly later than the part above (the proximal heart) with which it is now connected by a relatively narrow bridge of intact heart tissue. With further narrowing of the connecting bridge a stage may be obtained in which the distal heart fails to contract with every other beat of the proximal heart. The rate of the latter is to that of the former as 2 is to 1; to apply a term that has come into general use, the rhythm is 2 to 1. Higher grades of block, 3 to 1 and 4 to 1 rhythms, may also be obtained, but, with further cutting, the block to the passage of the impulse soon becomes complete despite incomplete anatomical separation of the two parts of the heart. The impulse starting in the more rhythmical parts of the heart can no longer reach the distal heart, and the latter, therefore, ceases to beat until it can, in case it beats at all, develop its inherent rhythmicity. Its rate of beat is then always slower than that of the proximal heart, it matters not through what level of the heart the

[1] Read by invitation at a meeting of the Section on General Medicine of the College of Physicians of Philadelphia, January 13, 1908.

[2] Jour. Physiol., 1883, iv, 43.

cut may have been made. A similar stoppage of the distal heart with subsequent development of rhythm is seen when the cut is completed rapidly. Then, of course, none of the intermediate stages of block intervene. (2) The impulse may be blocked if instead of cutting the heart tissue, it be gradually compressed in a clamp.[3] Identical results are obtained with both methods.

These experiments teach (*a*) that the upper parts of the cold-blooded heart are more rhythmical than the lower, (*b*) that the pace of the whole heart is normally set by the upper more rhythmical parts, and (*c*) that at the moment a less rhythmical part of the heart is severed physiologically from a more rhythmical part, the former at first stops beating and then, in case it possesses the property of automatic rhythmicity, it gradually assumes this function and begins to beat, otherwise it remains quiescent indefinitely.

Since the slightest obvious interference with the conduction of the impulse between any two parts of the heart manifests itself as an interval between the beats of such parts, Gaskell has concluded that in the normal heart the perceptible interval between the beats of the several chambers, sinus and auricles, auricles and ventricle, must be due to the existence in their junctions of a natural block to the passage of the impulse. The heart tissue in these places, he has pointed out, differs in structure and arrangement from those parts of the heart tissue that constitute the walls of the several chambers. These differences, in his opinion, suffice to account for the delay in the transmission of the impulse from chamber to chamber.

It is not a difficult matter to picture to ourselves in the case of the cold-blooded heart the irregularities of heart beat due to experimentally disturbed conductivity. Furthermore, the heart of cold-blooded animals lends itself well to experiments of the kind described above. Not only is it relatively simple structurally in that developmentally it is not far removed from the simple primitive heart tube, but in addition the heart possesses such a high grade of automatic rhythmicity that it may be removed from the organism and experimented upon as described and still continue to beat.

The conditions with which the experimenter has to deal in the case of the warm-blooded heart and particularly in the case of the mammalian heart are not quite so simple. Nevertheless, when due allowance is made for differences in structure and when appropriate methods of experimentation are employed, it can be shown that interference with the conduction of the excitation wave has much the same effects upon the heart beat in both classes of animals.

Structurally the mammalian heart differs materially from the cold-blooded heart. An anatomically distinct sinus venosus no longer exists, and there are present in it two completely separated auricles

[3] Gaskell, Philosophical Trans., pt. III.

and ventricles. Since, however, the mammalian heart is evolved from the cold-blooded heart it should be possible for embryologists to determine their analogous parts. The problem is an old one. Very recently, however, Keith and Flack,[4] stimulated, apparently by the active interest taken in the subject by physiologists and experimental pathologists, have studied very carefully the comparative anatomy of the human heart and especially of those parts of the human heart which correspond with the junctions in the more primitive types. The results recorded are of the greatest interest and value to students of the manifestations of disturbed conductivity in the heart of man, and we may, therefore, be justified in quoting at some length the significant conclusions of their research.

Keith and Flack first call attention to the fact that from the standpoint of comparative anatomy the typical mammalian heart may be divided into (1) the sinus venosus, (2) the auricular canal, (3) the auricle, (4) the ventricle, and (5) the bulbus cordis. "In the human and mammalian heart the musculature of the auricular canal has grown over and submerged the greater part of the sinus; two parts only are left exposed on the surface of the heart: (1) The musculature of the superior vena cava, and (2) the musculature of the coronary sinus." But on section "a second or deep stratum of the musculature is seen; this probably belongs to the sinus venosus, since it extends beneath the endocardium of the auricle, from the position of one venous valve to that of the other." There is also a part of the musculature "in the Thebesian and Eustachian valves, these being remnants of the right venous valves. There is often also to be found a thin muscular layer along the lower border of the fossa ovalis. . . ." All of these remnants of the sinus are in the right auricle. "It may be, however, that there are also remnants of the sinus in the left auricle of the human heart" around the orifices of the pulmonary veins. "Thus in the right auricle of the human heart there is musculature derived from three sources: (1) From the auricle proper, (2) from the auricular canal, (3) from the sinus venosus. . . . . All of these parts are in the freest muscular continuity."

"In the mammalian heart a distinct remnant of the sino-auricular junction, so well shown in more primitive hearts, can be recognized." Thus "in the human heart . . . an artery or arterial circle lies in the junction; the artery is surrounded by fibrous tissue in which are numerous peculiar muscle fibers, some nerve cells, and nerve fibers." "The muscle here has a structure quite similar to that of the auriculoventricular bundle."

The question whether there exists an anatomically distinct junction between the musculatures of the auricles is not considered by Keith and Flack. But all anatomists, so far as I am aware,

[4] Jour. Anat. and Physiol., 1907, xli, 172.

describe direct continuity of a large part of the muscle fibers of the two auricles.

It is hardly necessary to refer here, owing to the interest Philadelphians have taken in this subject from the very beginning, to the recent researches on the anatomy of the auriculoventricular junction. That the auriculoventricular bundle constitutes the only bit of heart tissue joining the heart tissue of the auricles with that of the ventricles is a fact that is now universally accepted. Keith and Flack describe the auriculoventricular bundle as a system of fibers which "begins in the '*knoten*,' a small mass of interwoven fibers in the central tendon of the heart, having slender connections with (1) the musculature of the interauricular septum, and (2) the circular fibers of the right auricular canal. From this arises the main bundle which passes along the upper border of the interventricular septum below the *pars membranacea septi*. Here it divides into a right and a left division which pursue a subendocardial course in the right and the left ventricles respectively, and, finally, fuse with the ventricular muscle."

There is no line of demarcation between the musculatures of the two ventricles. The work of MacCallum[5] has demonstrated conclusively that the ventricles, "instead of being a complex of fibers running at random, is merely a simple, long band of muscle with a tendon at each end as in other muscles." This band has its origin in the connective tissue of the auriculoventricular junction upon one side of the heart, passes around the outer wall of that side, thence to and through the ventricular septum, encircles the outer wall of the other ventricle and terminates in the *chordæ tendinæ* of that side. The musculature of the ventricles has therefore the arrangement of a scroll, and we may assume, in the absence of definite investigations upon this point, that the fibers of the auriculoventricular bundle make connection with the centre of the scroll.

Functionally the main difference between warm and cold-blooded hearts, from the standpoint of the experimenter, consists in the dependence of the former upon the coronary circulation. For physiological purposes the mammalian heart must be studied either while retaining its natural relation to the organism or when, after excision, its beat is maintained by the perfusion of its coronary system.

The studies of the anatomy of the mammalian heart outlined above should suggest to the investigator acquainted with the physiology of the cold-blooded heart that in the heart of mammals there are in all probability two natural blocking points: one at the junction of the rudiments of the sinus with the auricles (mainly in the right auricle), the other at the junction of the auricles with the ventricles, provided it can be shown that the impulse that causes the

[5] Johns Hopkins Hosp. Rep., 1900, ix, 307.

heart to beat starts in the sinus and traverses the auriculoventricular bundle; and it might be justifiable to infer further upon the same premise, that the natural block at the auriculoventricular junction is the more efficient. Practically all of these inferences have been justified by the test of experiment and it is with the results of such experiments that this paper principally deals.

The influence upon the heart beat of the block, both natural and experimental, has been studied most thoroughly in connection with the auriculoventricular junction, and we may therefore begin the physiological section of this paper with the presentation of the clearest subject. At the outset it may not, perhaps, be superfluous to state that the auriculoventricular bundle constitutes the only functional connection between the auricles and the ventricles of the mammalian heart. When this bundle, or practically nothing but it, is transsected in the excised artificially perfused heart[6] or when it is crushed in the heart retaining its normal relations to the organism,[7] the ventricles usually come to rest at once, whereas the auricles continue to beat with undisturbed rate and rhythm. Soon, however, the ventricles begin to beat, slowly at first, but the rate of beat gradually increases to a constant one which is, even when fully developed, always slower than that of the auricles. Now the auricles and ventricles beat quite independently of each other; the latter more slowly than the former. The justifiable inferences from these experiments are: (1) That the pace-maker of the mammalian heart is not in the ventricles (after section of the heart tissue the proximal heart beats more rapidly than the distal)—it lies either in or above the auricles; (2) that the ventricles of the mammalian heart are automatically ryhthmical, but that while they are driven by the auricles their rhythmicity is held in abeyance—it develops gradually when they are thrown upon their own resources. Furthermore, the pause between the contractions of auricles and ventricles of the normal heart (As-Vs interval) is satisfactorily accounted for by the fact that the impulse, in passing from one to the other of these regions, must traverse a long narrow bridge.

On account of the minuteness of the auriculoventricular bundle its conductivity cannot well be gradually impaired by slowly cutting into it. It may, however, be so impaired by gradually compressing it in a specially devised clamp applied to the normally beating heart.[8] In this way all grades of impaired conductivity, such as we have described in connection with the cold-blooded heart, may be obtained. These, in order of their appearance, consist of (1) an increase in the

[6] His, Jr. Zntrbl. f. Physiol., 1895, ix, 469. Humblet: Arch. intern. de physiol., 1904, i, 278. Hering (read March 10, 1905), Prager med. Wochenschrift, xxx, No. 14; also, Pflüg. Arch. 1905, lvii, 97.

[7] Erlanger (read March 20, 1905), Bull. Johns Hopkins Hosp., 1905, xvi, 202; also, Jour. Exp. Med., viii, 8. v. Tabora: Ztschr. f. exp. Path. und Therap., 1906, iii, 499.

[8] Erlanger. loc. cit.

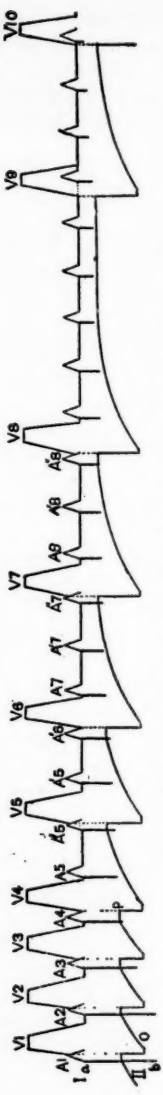

FIG. 1.—Diagram to illustrate the genesis of heart block. For description see text.

As-Vs interval. (2) The occasional failure of the ventricles to respond to the regularly contracting auricles—these "ventricular silences" may recur with great regularity, for example, after every tenth, ninth, or eighth, etc., auricular contraction. (3) The failure of the ventricles to respond to every other auricular contraction—a 2 to 1 auriculoventricular rhythm. (4) A 3 to 1 rhythm. (5) Relatively complete auriculoventricular heart block (of which more in a moment). (6) Absolutely complete auriculoventricular heart block. These several disturbances in conductivity I have attempted to make clear by means of a diagram[9] (Fig. 1) based in part upon experimentally demonstrated facts, in part upon logical inferences from such facts. In the figure the line I shows diagrammatically the movements of the heart, A1, A2, A3, etc., being the contractions of the auricles; V1, V2, V3, etc., the contractions of the ventricles. Line II represents diagrammatically the variations in the irritability of the ventricles. It is an old observation, one dating from 1876,[10] that with each contraction of heart tissue its irritability is completely annulled. During the phase of contraction heart tissue does not respond to stimulation, but during the phase of relaxation and during the pause following it the irritability returns and then gradually increases. The increase, rather rapid at first, becomes slower and slower as the irritability approaches its maximum level. The curve of irritability included between successive ventricular contractions tends, therefore, to approach the level of maximum irritability asymptotically, that is to say, it tends to become parallel to the base line. These variations in the irritability of heart muscle are explained as follows: The resting heart tissue stores within itself an unstable energy yielding material, the instability of which increases as it accumulates. A stimulus strong enough to elicit a contraction does so by decomposing all of this material. The irritability of the heart tissue, it may be assumed, depends

[9] Erlanger. Amer. Jour. Physiol., 1906, xvi, 160.
[10] Marey. Trav. d. Lab., 1876, 73.

upon the amount of the unstable substance present in it at any one time. Immediately after the heart has contracted it, therefore, contains none of the unstable substance; consequently it is non-irritable. But after the heart has completed its contraction the material begins to accumulate rapidly at first and then more and more slowly; the irritability, when it returns, therefore increases rapidly at first but finally becomes more or less constant. Or stated in another way, shortly after the completion of a contraction, a stimulus to be efficient must be relatively strong, but as time passes a relatively weaker stimulus becomes effective. Indeed what has been termed the inner stimulus may, in case the heart tissue is not otherwise disturbed, become efficient and cause the heart to beat spontaneously. It is justifiable to assume further, that the strength of the impulse starting in any part of the heart depends upon the amount of the unstable material decomposed by the contraction associated with it. In other words, the strength of the impulse in general varies with the interval between contractions. Finally the latent period of contraction of heart tissue varies inversely as the strength of the stimulus producing the contraction, and inversely as the irritability of the heart tissue. That is to say, a relatively strong stimulus produces a contraction with a short latent period, while in the case of a stimulus of a given strength acting upon a more or less irritable tissue, the resulting contraction will in the former case have a short latent period, in the latter a long latent period.

I do not wish to give the impression that the factors taken into consideration in the development of this theory are the only ones that play a part in determining the behavior of the heart toward interference with the transmission of the contraction wave through it. Although, apparently complex, it is the simplest explanation of the complex manifestations of heart block and it is hoped that it may prove as useful to the clinician as it has to me as a working hypothesis in the elucidation of the phenomena of heart block.

The diagram depicts the results of gradually clamping the auriculo-ventricular bundle. Pressure exerted upon the bundle will have the effect of reducing the efficiency of the auricular impulse that reaches the ventricles. The efficiency of this impulse is represented by the length of the heavy line dropped from the foot of the auricular wave. It is assumed that this impulse is efficient whenever the line representing it intersects the curve of irritability of the ventricles (II). A ventricular contraction then results. The duration of the latent period of the ventricular contraction is represented by the length of the horizontal line at the crest of the waves of irritability (on II).

We are now in a position to explain with the aid of the diagram the various grades and phases of disturbed conductivity at the

auriculoventricular junction. The first two cardiac cycles[11] are normal. The impulse (*ab*) descending from the auricles (A1 and A2) into the ventricles are much stronger than a barely efficient one. The latent period of ventricular contraction is short.

The rest of the diagram depicts some of the effects of gradually clamping the auriculoventricular bundle. The first effect is to diminish the strength of the impulse (line descending from foot of A3); it is still, however, efficient (intersects the curve of irritability of the ventricles II), but, the stimulus being weaker, the latent period of contraction of the ventricles—the As–Vs interval—is longer. The same is true in the case of the fourth cardiac cycle (A4, V4) the only difference being a still greater divergence from the normal. The auricular impulse (A5) of the fifth cardiac cycle (A5, A′5, V5), owing to the increase in the resistance to its passage through the auriculoventricular bundle, does not reach the curve of irritability of the ventricles; in other words this impulse is subminimal. The ventricles, therefore, do not contract and their irritability instead of falling to O continues to increase. On account of this increased irritability the impulse associated with the next auricular beat (A′5), although no stronger than that of A5, is efficient and the ventricles contract. The latent period of the ventricular contraction is shorter than that of the preceding one (V4) for the reason that the irritability of the ventricles is higher while the efficiency of the auricular impulse (A′5) is still relatively great. A continuance of this state of affairs would result in a lasting 2 to 1 auriculoventricular rhythm. A slightly greater block to the passage of the impulse through the auriculoventricular bundle may so alter the relation of efficiency of impulse to irritability of ventricle that the rhythm becomes 3 to 1. This is shown in cycles 7 and 8 in the diagram. Rarely, however, are higher rhythms, 4 to 1 and 5 to 1, seen in the mammalian heart. The reason for this, illustrated in the diagram, is to be found in the fact that although the auricular impulses may succeed in penetrating into the ventricles they always remain subminimal with respect to the irritability of the ventricles. They therefore cease beating until their inherent stimulus suffices to originate a contraction, when they beat automatically and quite independently of the auricles. We now have before us the condition that was termed above relatively complete block. It is relatively complete because the degree of block depends upon the efficiency of auricular impulses in relation to the irritability of the ventricles. If we could by some means increase the irritability of the ventricles the block might become partial again; so, too, might the block become partial if we could increase the efficiency of the auricular

[1] It is convenient for our purposes to define cardiac cycle as those events that intervene between the beginning of an auricular contraction immediately following a ventricular contraction, and the beginning of the auricular contraction immediately following the next ventricular contraction.

impulses. As a matter of fact it does lie within our power to vary the strength of the auricular impulse. This, we have assumed above, may be accomplished by altering the rate of the auricular beats, an increase in rate being associated with a diminution, and a decrease in rate with an increase in the efficiency of the impulse. In the latter case, for example, the impulse of the third or fourth auricular contractions following V8 might have become efficient stimuli. Then the block would have become partial, and in the former case the efficiency of the auricular impulse A″8 might have fallen below that required for stimulation of the ventricles, and the partial block then existing might have become relatively complete. The arrhythmias associated with other forms of heart block are easily comprehended when viewed in the light of this hypothesis.

SINO-AURICULAR HEART BLOCK. So far as I am aware a condition that might unequivocally be termed sino-auricular heart block has never been experimentally produced. Nevertheless the anatomical description of the heart given above would seem to indicate the possibility of there being another natural blocking point at the sino-auricular junction. Although there is in this place no narrow muscular bridge such as is found at the auriculoventricular junction still we find here interpolated between the sinus and the auricle a peculiar heart tissue. We find very little more than this at the sino-auricular junction of the cold-blooded heart, and yet most physiologists, following the lead of Gaskell, believe that it suffices to account for the S;s–As interval in that heart; it, in other words, acts in that heart as the natural block to the passage of the impulse. And it seems to me possible that under pathological conditions, such for example as occlusion of the artery lying in the sino-auricular junction of the mammalian heart, the tissue in this junction might be so impaired functionally as partially or completely to block the passage of the impulse.

However that may be, the question presents itself for consideration: Is there any evidence that in the mammalian heart the impulse arising in the *primum movens* (assuming this be in the mouths of the great veins) is materially delayed in the sino-auricular junction? In the present state of our knowledge this question cannot be answered. None of the recent workers in this field has, so far as I am aware, succeeded in satisfactorily recording the contractions of the superior vena cava simultaneously with those of the auricles. And since, according to Keith and Flack, the superior vena cava is the only part of the sinus of the mammalian heart that is not incorporated within the tissue of the auricle, the problem of determining by direct methods the duration of the normal S;s–As interval, if such interval there be, seems to be impossible of direct solution.

Another question then suggests itself, namely: Is it possible artificially to block the passage of the impulse through the region of the mammalian sinus, using for this purpose methods similar to those

employed by Gaskell in his study of conduction in the cold-blooded heart? That this can be accomplished has been demonstrated by experiments which, although indirect, are I believe none the less conclusive.[12] A block has been established in the following way: The heart of a rabbit is excised and perfused with Locke's solution. A heavy thread is passed through the right auricle entering by way of the inferior vena cava and leaving by way of the superior. After the heart has begun to beat normally gentle traction is exerted upon the projecting ends of the thread so as to elevate a cone of auricular tissue. Naturally this cone includes the mouths of the great veins and a variable amount of the tissue of the right auricle bordering upon them. While holding the thread taut the two projecting ends are twisted one upon the other. The torsion is, of course, not limited to the thread, but is continued to the auricular tissue drawn up by it. In this way, therefore, a large part if not all of the sinus region of the auricles is compressed, the greatest tension being exerted, however, upon the base of the cone. It is impossible in an experiment of this kind to record or even to see the contractions of the part of the heart twisted. Nevertheless by these means an irregularity of heart beat has been repeatedly obtained which, when viewed in the light of the remarks of the preceding section, could be caused only by the interposition of a block in the way of the impulse from a more rhythmical to a less rhythmical part of the heart. When the torsion is quickly exerted upon the sinus region of the right auricle the whole heart may apparently cease to beat just as the ventricles may cease beating when an auriculoventricular block is suddenly established. After a variable pause (in Fig. 2 the first pause lasts about six seconds) the heart may contract with normal sequence, that is, auricles first, followed in a moment by ventricles. Then there succeeds a shorter pause followed by another apparently normal contraction and so on until a constant but slow rate obtains. This period of the experiment corresponds with the development of rhythm in the ventricles after the establishment of complete auriculoventricular block, and without doubt some part of the heart without the twisted area is here developing the rhythm that determines the beat of the auricles and ventricles in lieu of the *primum movens* which the operation has rendered functionless with respect to the rest of the heart.

The constant but slow auriculoventricular rate that next obtains is in all probability the expression of complete sino-auricular block. Now, in case the treatment to which the auricle has been subjected has not permanently damaged the tissue concerned with the origination of the normal beat, the heart will, when the tension is removed, slowly but completely resume its normal state. At first, during such recovery, the visibly beating portions of the heart may

[12] Erlanger and Blackman. Amer. Jour. Physiol., 1907, **xix**, 125.

contract at intervals almost exactly equal to thrice the normal period, evidently 3 to 1 sino-auricular block, and then there may be seen in successive stages sino-auricular block of alternating 3 to 1 and 2 to 1, 2 to 1, alternating 2 to 1 and 1 to 1, and, finally, the normal 1 to 1 rhythms (Figs. 3, 4, and 5). That is to say, the heart periods will in the first case be alternately equal to three and two normal periods, then to two normal periods, then alternately to one and two normal periods, while, finally, the heart may beat just as it did before its rhythm had been disturbed. These irregularities, even in the absence of any direct evidence that some part of the heart above the assumed block is throughout the experiment beating at the normal rate, practically prove, in the light of the hypothesis developed above, that such is actually the case. The experiment then suggests that the *primum movens* is situated above the lowermost edge of the twisted part of the auricle. That such is the case is indicated by the fact that in the dying heart, this is the part of the heart which may show the last contractions. It is likewise the part that may first begin to beat when the quiescent heart is perfused.[13] And in at least one of the several experiments the cone of the auricles picked up by the thread, after having been separated functionally from the rest of the heart, by means of a crush through its base, was seen to beat more rapidly than, and independently of, the other parts of the heart.[14]

Sino-auricular heart block, or at least partial sino-auricular heart block, is characterized then by the occurrence of heart cycles whose durations are simple multiples of that of the normal heart cycle. Admitting this to be a correct criterion, then partial sino-auricular heart block has been casually observed in man by Wenckebach[15] and in the dog by Hering.[16] In neither case could the exact cause of the arrhythmia be determined.

Auriculo-auricular Heart Block. The term auriculo-auricular heart block is self-explanatory. It is a condition in which the conductivity of the tissue joining the two auricles is depressed to such an extent that the impulse that causes the heart to beat is blocked either partially or completely on its way from one to the other auricle. Experimentally the impulse may be so blocked in the excised heart of the rabbit either by a line of crush or by means of actual separation with scissors.[17]

I shall consider first the effects of the functional separation of the right auricle from the left auricle plus auricular septum by means of a cut parallel to, and just to the right of, the line of junction of the auricular septum with the vault of the auricles. Let this cut be so planned that there is left between the two auricles a bridge of uncut

[13] MacWilliam: Jour. of Physiol., 1888, ix, 167. Hering: Pflüger's Arch., 1900, lxxxii, 21. Fredericq: Arch. intern. d. physiol., 1906, iv, 57. Erlanger and Blackman: Loc. cit.
[14] Erlanger and Blackman. Loc. cit.
[15] Ztschr. f. exp Path. u. Therap., 1906, 511.
[16] Arch. f. Physiol., 1906, 297
[17] Erlanger and Blackman. Loc. cit.

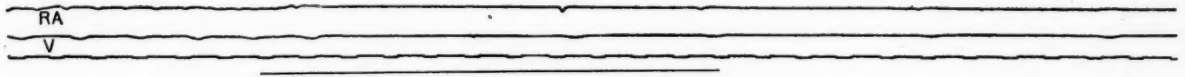

FIG. 2.—To show the production of, and the different stages of recovery from, complete sino-auricular block resulting from the twisting of the region of the great veins. Before, there was a 2 to 1 auriculoventricular block. The duration of torsion is indicated by the line just below the time record. Time-interval between two symmetrical marks is one second. Down strokes are contractions. Rabbit.

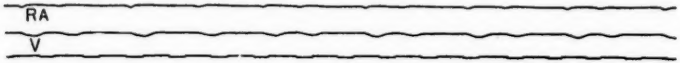

FIG. 3.—Shows the change from a sino-auricular block of the 2 to 1 type to a block of the alternate 2 to 1, 1 to 1 type. Now, none of the auricular impulses are blocked at the auriculoventricular junction

FIG. 4.—Shows alternate 2 to 1 and 1 to 1 sino-auricular block.

FIG. 5.—Shows the return to normal sequence from an alternate 2 to 1 and 1 to 1 sino-auricular block.

auricular tissue which, however, is damaged to such an extent that impulses cannot at first make their way across it from one auricle to the other. At the moment this is accomplished the left auricle and auricular septum may at once come to rest, whereas the right auricle continues to beat with undisturbed rate. After a short pause, however, the left auricle with attached septum begins to beat, perhaps slowly at first, but more rapidly later when its rhythmicity is fully developed. Then the left side contracts regularly, but more slowly than, and independently of, the right (Fig. 6). We have here, to coin a word, complete dextauriculo-septolevauricular heart block. Subsequently, with the gradual disappearance of the block, there occur in turn the several stages of partial block such as 3 to 1 dextauriculo-septolevauricular heart block when the left auricle plus septum contracts after every third beat of the right auricle, 2 to 1 block (Fig. 7), and then perhaps the normal rhythm with a perceptibly long interval between the contractions of the right and of the left auricle, or as we might call it by analogy, a long dAs-SelAs interval, and finally the heart beat becomes absolutely normal.[18]

The auriculoventricular bundle, the physiological connection between the auricles and ventricles, lies, as we have seen, in the septum. The beat of the ventricles in an experiment of the kind just described is determined, therefore, by the beats of the auricular septum, and since the connection of the left auricle with the septum is undisturbed, the left auricle and the ventricles beat with the sequence that obtains in the intact heart.

The experiments upon sino-auricular heart block described above proved the most rhythmical part of the heart to be in the right auricle in the region of the mouths of the cavæ. The experiment just described confirms this finding in that it shows the right auricle to possess a higher degree of rhythmicity than the left auricle plus the auricular septum. In addition the experiment demonstrates that the left auricle plus the septum like the right auricle and the ventricle is automatically rhythmical; for in the case of complete separation of the two parts both beat, although independently of each other—the left side always more slowly than the right.

Let us consider next the effect of separating functionally the left auricle from the right auricle plus the auricular septum, altering the method described above only in so far as the position of the cut is concerned. In this case the cut is carried through the vault of the auricles just to the left of, instead of just to the right of, the septum. The left auricle usually stops beating at the moment the functional separation becomes complete, whereas, the right auricle and septum continue to beat without the slightest change in rate (Fig. 6). The left auricle in a vast majority of experiments does not beat again as long as the functional separation is complete. In this respect the

[18] Wenckebach (loc. cit.) has obtained from man tracings which he believes show the right auricle to be beating independently of the rest of the heart.

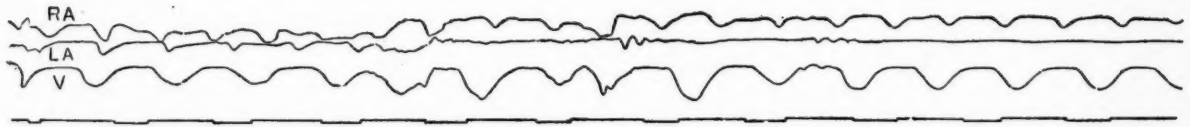

FIG. 6.—Shows at the beginning complete blocks between the right auricle and the left auricle plus the septum, and between the latter and the ventricles. Later (at irregularities), the left auricle was separated from the auricular septum and stopped beating at once. Down strokes are contractions. Rabbit.

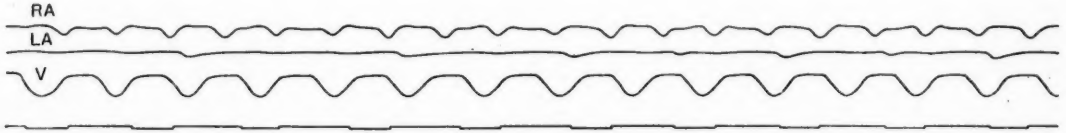

FIG. 7.—Shows the ventricles beating independently and the left auricle responding at first to every fourth contraction of the right auricle, then to the third, and then to every second to the end of the tracing. Down-strokes are contractions. Rabbit.

separation on the one hand of the left auricle and upon the other of the left auricle plus the septum from the right yields different results. The difference is due to the fact that, whereas, the left auricle plus the septum possesses automatic rhythmicity, the left auricle alone does not or possesses it to but a slight degree. Evidently the septum alone is automatically rhythmical since it is the part of the heart that determines the beat of the left auricle when together they are separated from the right. That the septum is automatically rhythmical may be proved by the direct experiment of separating it from both of the auricles by cuts through the vault to either side of it. Then the septum may be seen to beat independently of the two auricles and to determine the beat of the ventricles, while the right auricle beats more rapidly than it, the left auricle remaining quiescent.

To complete the consideration of the effects of separating functionally the right auricle plus the septum from the left auricle, as the conductivity of the connecting bridge gradually returns and the impulse of the right auricle succeeds in penetrating into the left, the various stages of partial block make their appearance. And we may, therefore, see 3 to 1, 2 to 1, etc, septodextauriculo-levauricular heart block.

Many other forms of heart block have been produced in the laboratory, but those which have been described here in barest outline are the ones which, for anatomical reasons, ought to be of the most frequent occurrence in the experience of the clinician. Just as partial and complete block may be established experimentally between any two parts of the heart, provided one of the parts be spontaneously rhythmical, by narrowing the functional connection between them, so, too, the same forms of block might well be produced by pathological processes of a kind that severs the functional connection of one part with another. When a transitory block is thus established by a lesion to repeat, the less rhythmical part at first stops beating but, in case it possess spontaneous rhythmicity, it soon begins to beat again, first in complete block and then in partial block with all of the rhythms that have been observed for example in the transitory auriculoventricular block. Naturally, auriculoventricular block of all the forms will be found to be, and has been found to be, the most common clinically, not alone for the reason that the narrowness of the connection between the auricles and the ventricles makes easier its partial and complete destruction by disease, but also because the clinical manifestation of auriculoventricular heart block (Stokes-Adams disease) are unmistakable. While it may be possible in particularly clear cases of auriculoventricular heart block to make a correct diagnosis without the aid of the more exact methods of investigating the organs of the circulation, the more obscure cases of this form of heart block, but especially the other forms of heart block, can be recognized only with the aid of the graphic method.

AN OBSERVATION ON THE JUGULAR PULSE OF MAN.[1]

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The revival of interest in the venous pulse of man, following the publication of James Mackenzie's[2] work, has, as a natural result, given rise to considerable discussion as to the cause and significance of the various waves which go to make up the venous pulse. Controversy arose over the first or auricular wave of the jugular pulse, the *a* wave of Mackenzie, while the origin and time of the third large wave, Mackenzie's *b*, occasioned even greater dispute. The second wave of the jugular pulse, wave *c*, which interrupts the first negative phase after the auricular wave, was formerly ascribed to numerous causes; after Mackenzie's publication, however, these seemed disposed of and his explanation, namely, that wave *c* was due to the impact of the neighboring carotid, was generally accepted. As recently as the early part of 1906, Wenckebach,[3] in an exhaustive article on the venous pulse, stated that he agreed with Mackenzie and all other recent writers in regarding the wave called *c* as chiefly a carotid product. Today such unanimity no longer obtains, since within the last year Leon Fredericq[4] and Morrow[5] have sought to disprove the carotid origin of the wave *c* and, more recently, Bard,[6] Cushny and Grosh,[7] and Hirschfelder[8] have expressed a like doubt.

Briefly stated, the arguments in favor of the carotid origin of wave *c*, as advanced by Mackenzie,[9] Wenckebach, and others, are: (1) Its time falls within the time of active ventricular systole, synchronous with the carotid pulse. (2) The size of this wave varies significantly according to the nearness of the pressure point of the receiving cup to the carotid artery, and according to the depth at which it is placed in the neck tissue. (3) The wave *c* is absent in the "liver pulse." (4) During irregular heart action, when the venous pulse continues and the arterial pulse is absent, in tracings

[1] Read by invitation at a meeting of the Section on General Medicine of the College of Physicians of Philadelphia, November 11, 1907.

[2] The Study of the Pulse. Edinburgh and London, 1902.

[3] Beiträge zur Kenntnis der menschlichen Hertztätigkeit. Archiv f. Anatomie und Physiologie, 1906, Physiol. Abtlg., p. 297.

[4] La seconde ondulation positive (première ondulation systolique) du pouls veinieux physiologique chez le chien. Bulletin de l'Académie Royale de Médicine de Belgique., 1907.

[5] The Various Forms of the Negative or Physiological Venous Pulse. Brit. Med. Jour., December 22, 1906, p. 1087.

[6] Des divers details du pouls veineux des jugulaires chez l'homme. Journal de physiologie et de pathologie générale. Paris 1906, viii, 466.

[7] The Venous Pulse. Jour. Amer. Med. Assoc., October, 12, 1907.

[8] Some Variations in the Form of the Venous Pulse. Johns Hopkins Hospital Bulletin, June, July, 1907.

[9] The Interpretation of the Pulsations in the Jugular Veins. Amer. Jour. Med. Sci., 1907, cxxxiv, 12.

of the jugular pulse taken at this time the carotid wave is not seen. (5) When there is a distended jugular bulb the *c* wave is not apparent in the venous tracing. (6) When the carotid wave is very prominent in a jugular tracing, its shape often is almost identical with that of a tracing of the carotid pulse. Although some of these observations have been challenged, as yet no adequate proof of their inaccuracy has been advanced.

It is a noteworthy fact that those observers who most vigorously oppose the accepted cause of wave *c*, almost without exception, have based their observations on experiments performed upon animals in which the jugular veins were dissected out and isolated. They lose sight of the fact that the *c* wave under discussion is one obtained from the surface of the neck of man, where the veins make their changes in volume felt in the overlying structures. It is evident, therefore, that comparison is being made between phenomena which are not identical.

Morrow took tracings from the exposed right jugular of a dog in which the right carotid had been clamped below the level from which the tracing was taken. The left carotid was taken simultaneously, but no cardiogram was made with which to compare the jugular tracings. In these tracings Morrow obtained a small wave following the auricular one and occurring at the time of the beginning of the carotid pulse. He assumed that this small wave was *c* and that, all carotid influence having been eliminated, it must be caused by some other factor. He advanced several theories as to its cardiac origin.

By far the most complete experimental work has been done by Leon Fredericq. On anesthetized dogs Fredericq exposed the carotid and external jugular, and, after the vein was protected from all transmitted pulsations, he recorded simultaneously tracings of the venous pulse and of the carotids and a cardiogram of the right heart. Immediately following the first or auricular wave he observed a small second rise, which he called *bc*, which in its time corresponded a little late with the first part of the up-stroke of the cardiogram, and more or less with the beginning of the carotid pulse.

Fredericq next demonstrated that *bc* occurred in tracings of the right auricle and superior vena cava near the auricle, and, further, that at this level the beginning of *bc* coincided with the beginning of the systole of the right ventricle, but preceded the beginning of the carotid pulse. From these facts he concluded, that, although *bc* is produced earlier at the heart than the arterial pulse, since the arterial pulse, *i. e.* the carotid pulse, travels 6 to 8 meters per second whereas the venous pulse travels only 2 meters per second, the arterial pulse overtakes the wave *bc* at the level of the neck. Hence the coincidence in time which is usually observed, a fact which Fredericq infers accounts for the seeming relation which exists between the *c* wave in the jugular pulse of man and the carotid

pulse. The other writers who doubt the carotid origin of *c* apparently base their doubts largely on the above-mentioned experimental work.

It is obvious that both Morrow and Fredericq effectually eliminated all possibility of the carotid influencing their jugular tracings, and they certainly demonstrated that in the neck veins of dogs, as Chauveau has shown for the horse, there is a wave following *a* which coincides with the beginning of ventricular systole. It seems, however, by no means proved that the usually prominent *c* wave of the jugular pulse of man, occurring at a time when ventricular systole is fully established, is identical with this small wave which occurs earlier in its relation to the cardiac cycle.

It seemed, therefore, important to determine, if possible, the presence or absence of a wave in the jugular pulse of man which should correspond in the time of its occurrence to the wave *bc* of Leon Fredericq; and thus, if found present, to demonstrate that this wave, which Fredericq and Morrow confused with the *c* wave, exists in man as well as in dogs and occurs along with and entirely independent of the carotid wave.

On examining a clear cardiogram, there will often be found a little notch on the up-stroke of the tracing. The interval between the exact beginning of the rise due to ventricular systole and the top of this notch represents that part of the ventricular systole during which the ventricular pressure is steadily being raised until the hitherto closed semilunar valves are opened and active systole begins. The notch marks the opening of the semilunar valves, and the interval before this occurs may be termed a *ventricular presphygmic period*, or, as it has been called by some, the "*Anspannungzeit.*" It will be noticed that the wave *bc* of Fredericq occurs during this period of the cardiogram.

Therefore, in seeking a like wave in man only those tracings were used in which, if not a clear ventricular presphygmic period (Anspannungzeit) occurred, at least a suggestion of one was present in the cardiogram, and in which the venous pulse was clear. Some difficulty was experienced, due to the fact that the exact beginning of ventricular systole is often difficult to determine accurately. Further, it must be borne in mind that as the ventricular presphygmic period is an event recorded at the heart itself, any event in the jugular pulse which corresponds to this period in the cardiac cycle must be represented on the tracings as occurring slightly later. Such retardation was observed by Professor Wenckebach and me, but our estimate of the time of the delay was less than that recently given by Hewlett.[10]

The tracings examined were taken from persons normal as to

[10] The Interpretation of the Positive Venous Pulse. Jour. Med. Research, October, 1907.

their cardiovascular systems, as well as from those with grave lesions of the heart or kidneys. A number of jugular tracings showed a second distinct wave following the *a* wave and preceding the *c* wave (Fig. 1). But, upon carefully measuring the exact time of this wave, it was found that often it coincided exactly with or actually preceded the ventricular presphygmic period.

Fredericq has shown that his wave *bc* was originated by the beginning of ventricular systole. He demonstrated that it was present when the auricles ceased contracting and the ventricles continued to beat; and that when ventricular contractions ceased

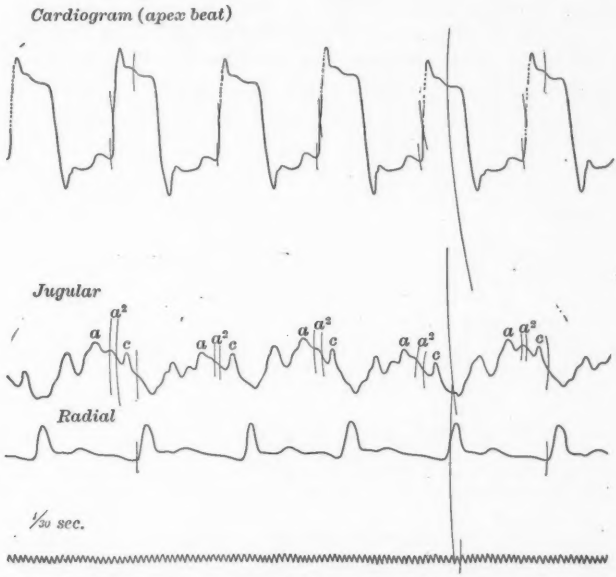

FIG. 1.—The jugular pulse shows the doubling of the auricular wave. The second rise of this (a^2) falls in or before the ventricular presphygmic period, which is indicated by the markings on the cardiogram.

the wave also disappeared in spite of auricular systole going on. It is evident, therefore, that those waves which in the tracings studied by me fell with or before the ventricular presphygmic period, could not be the same as Fredericq's wave, since, in the jugular pulse, at the period in question, that is before the ventricular presphygmic period, the influence of ventricular systole is not yet evident.

That a wave had to be dealt with which was in the nature of a double *a* wave seemed all the more certain, since in some cases of heart block a beautifully clear wave was found, which followed

immediately after the waves due to auricular systole, even when the latter were not succeeded by any ventricular contraction. Consequently, the influence of any ventricular systole as a factor in the cause of these double *a* waves was absolutely excluded in such cases. An illustration of this is seen in Fig. 2. It was evident, therefore, that care had to be taken not to confound a double *a* wave with the wave which was being sought.

The examination of other tracings revealed, in addition to this doubling of the *a* wave, still another small wave which fell just after or in the latter part of the ventricular presphygmic period, but invariably came before the beginning of active ventricular systole and hence preceded the *c* wave. Such a tracing is shown in Fig. 3, in which, at the bottom of a double auricular wave, a small but distinct wave is seen, designated by the letter *b*. By using the radial pulse as a means of comparing events in the jugular pulse and cardio-

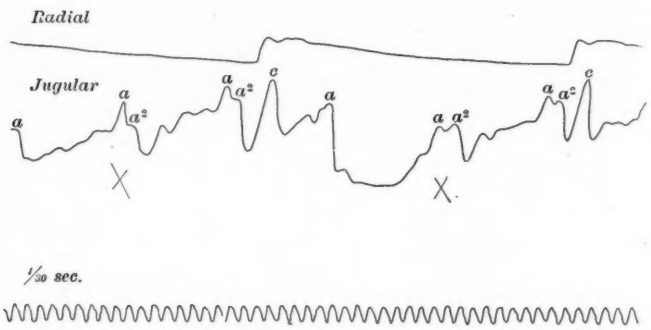

FIG. 2.—Heart block in which the jugular pulse shows a double *a* wave (a^2), even when the auricular contraction is not succeeded by a ventricular systole, as at (×).

gram, it is found that *b* occurs just after the ventricular presphygmic period. The foregoing seemed the proof that, aside from any double *a*, there exists in jugular tracings of man a small wave which corresponds in time to the wave found by Morrow and Fredericq in dogs, and which is clearly separate and distinct from the carotid wave (Mackenzie's *c*).

The occasional presence of the wave in question has been noted in a recent paper by L. Bard. In at least one of his tracings, he points out a wave in regard to the identity of which, with the one under consideration, there is little doubt. Bard called this wave *i*, but in view of the newer lettering of the venous pulse adopted by D. Gerhardt, Wenckebach, and others, in which one of the post-sphygmic waves is called *i*, it was suggested by Prof. Wenckebach that this small second wave of the jugular pulse of man might appropriately be called wave *b*. We should have, therefore, the

following convenient sequence of lettering: *a*, the auricular wave; *b*, the wave above described; *c*, the carotid wave; and *d*, the

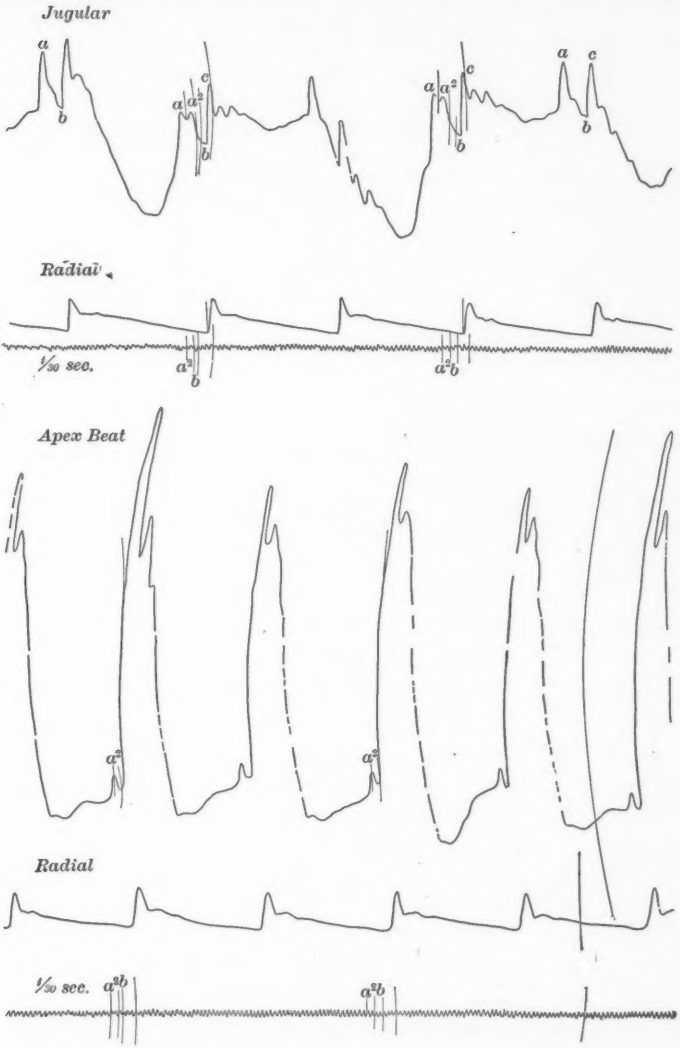

FIG. 3.—In the jugular pulse there occurs at the bottom of the double *a* wave another small wave, *b*. Wave *b* occurs just at the end of the ventricular presphygmic period and always precedes the beginning of *c*. The jugular pulse and the apex beat must be compared by means of the radial pulse.

diastolic wave of Wenckebach and Gerhart,[11] erroneously called *v*. The letter *v* should be reserved for such phenomena as occur during ventricular systole only. In a paper which appeared about

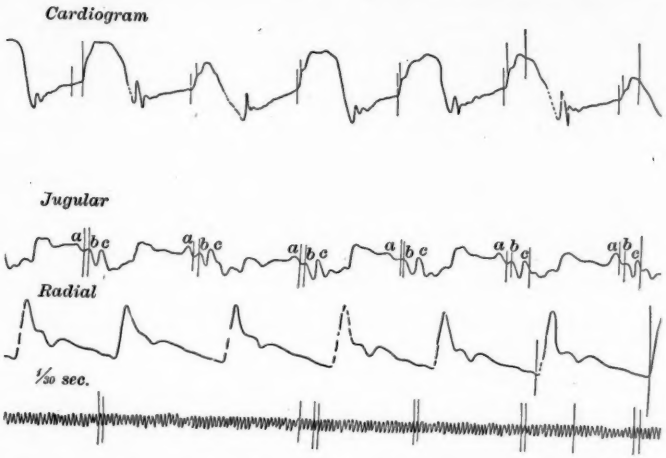

FIG. 4.—Wave *b* occurs as a distinct wave interrupting the down stroke of the *a* wave. It always occurs just after or in the last part of the ventricular presphygmic period, which is clearly shown on the cardiogram.

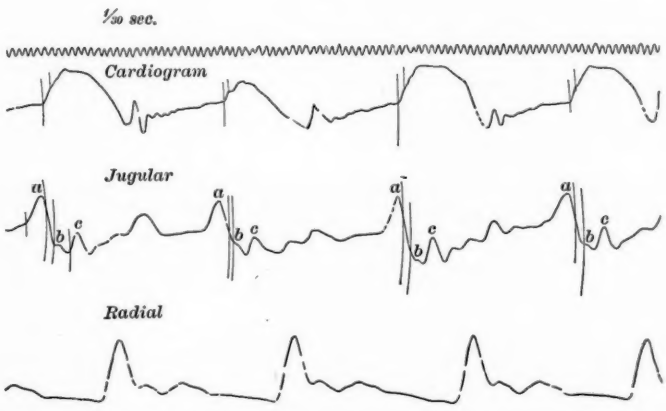

FIG. 5.—Wave *b* occurs just after the ventricular presphygmic period and is seen as a distinct elevation between the bottom of the down stroke of the *a* wave and the beginning of wave *c*.

[11] Klinische Untersuchungen über Venenpulsationen: Archiv. f. exp. Pathologie u. Pharmakologie, 1894, xxxiv, 402.

the same time as Bard's, Hirschfelder[12] makes no mention of the *c* wave as such, but describes, as the second wave of the jugular pulse, a wave similar in time to the above noted *b* wave; none of the tracings in this paper, however, seem to show a *b* wave.

The double *a* being of comparatively rare occurrence, the additional wave *b* was found most often following the usual single auricular wave. Its character was by no means constant, as may be seen from the accompanying series of tracings. In Fig. 4, *b* appears as a distinct wave interrupting the down stroke of *a*. In Figs. 5 and 6 an obvious wave is seen between the bottom of *a* and the beginning of *c*. Not infrequently *b* shows more as an outbowing on the de-

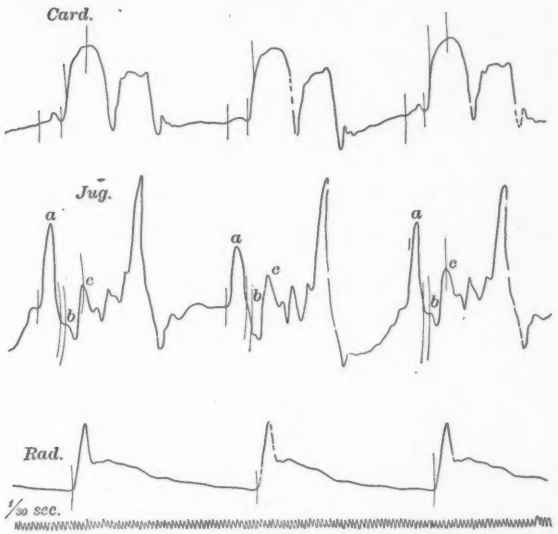

FIG. 6.—Wave *b* occurs at the bottom of the *a* wave when the latter follows a pause after an extra systole.

scending limb of *a* than as an abruptly rising wave. Of this type Fig. 7 furnishes an example. Again, there are tracings which show no clear *b* wave, but in which, during a distinct interval before the beginning of *c*, there is the suggestion of a small wave *b* (Fig. 8). Finally, *b* may appear as a wave at the beginning of the up-stroke of *c*. Fig. 9 shows this, although in this tracing the ventricular presphygmic period is not clear; nevertheless, *b* obviously falls in the first part of the systolic ventricular rise of the cardiogram. In spite of these variations as to form, the time of *b* remains unchanged. In

[12] Graphic Methods in the Study of Cardiac Disease. AMER. JOUR. MED. SCI., 1906, cxxxii, 378.

FIG. 7.—Wave *b* appears on the down stroke of the *a* wave more as an outbowing than as an abruptly rising wave, but its relationship to the ventricular presphygmic period is always correct.

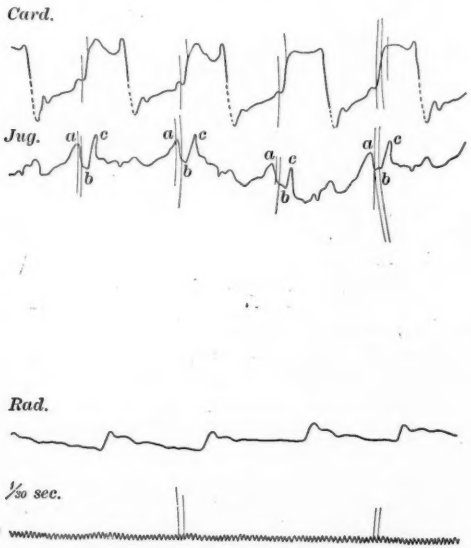

FIG. 8.—There is no distinct *b* wave in the jugular pulse, but in the interval between the end of *a* and the beginning of *c* the suggestion of one is evident.

the tracings examined it always occurred just after or in the last part of the ventricular presphygmic period.

This wave *b* is always small and by no means apparent in all jugular tracings, but when present can be no mere accident, since it is observed not only throughout a single tracing, but in repeated tracings from the same individual, even when they are taken on different occasions. Its occurrence is probably somewhat dependent upon the length of the *a-c* interval and the prominence of the *c* wave.

The cause of wave *b*, in the absence of definite experimental proof, remains a matter of speculation, although there seems no good reason for not accepting the suggestion of Leon Fredericq, namely, that

FIG. 9.—Wave *b* appears as a distinct elevation on the first part of the ascending limb of wave *c*. Although the ventricular presphygmic period is not clear in the tracing, wave *b* obviously falls in the early part of the systolic ventricular rise of the cardiogram.

this wave is due to the augmentation of the intraventricular pressure before the opening of the semilunar valves, and that this increased pressure communicates itself to the contents of the auricle across the auriculo-ventricular orifice closed at this moment by the tricuspid valves whose leafletts bulge toward the right auricle. Bard gave a like explanation of the cause of his wave *i*, and Hirschfelder attributed the second wave of the venous pulse to these same factors.

From the foregoing considerations the following conclusions seem warranted:

1. There are not sufficient grounds to doubt that the *c* wave in the jugular pulse of man is, as Mackenzie said, anything but a carotid product.

2. The jugular pulse of dogs, even when all carotid influence is eliminated, shows a small wave at the beginning of ventricular systole.

3. In man a double *a* wave is sometimes found, the second rise of which cannot be identical with the wave described in dogs, since its occurrence is too early.

4. In addition to any double *a* wave in man, another wave, appropriately called wave *b*, often shows between *a* and *c* and begins just after or in the last part of the ventricular presphygmic period.

5. Since the wave found in the jugular pulse of dogs at the beginning of ventricular systole has its counterpart in the *b* wave of man's jugular pulse, the assumption that the wave found in dogs is identical with Mackenzie's *c* wave is unjustifiable.

I gratefully acknowledge the many kindnesses shown me by Prof. K. F. Wenckebach, at whose suggestion this work was undertaken. In addition to the admirable facilities afforded in the Laboratory of Clinical Medicine at Groningen, Prof. Wenckebach generously placed at my disposal for study a large series of tracings, which, together with those that I made myself, supplied the material for the observations above recorded.

PRIMARY CARCINOMA OF THE VERMIFORM APPENDIX.

A STUDY OF 90 CASES, 3 PREVIOUSLY UNPUBLISHED.[1]

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The increasing reports of isolated cases of primary carcinoma of the appendix, which one finds in the literature, testify not only to the greater interest now manifested in the study of the pathological anatomy of that organ, but also to the greater care exercised in its examination, whether removed at operation or on the autopsy table. A sufficient number of such neoplasms have now been recorded to make a critical study of them interesting and instructive. To the 87 cases that I have found reported in the literature, I desire to add the following 3 cases:

Case XXII.—An unmarried, German, immigrant girl, aged twenty years, was admitted, on September 5, 1907, directly from the steamer to the Presbyterian Hospital, to the service of Dr. F. T. Brown, to whom I am indebted for the privilege of taking care of

[1] The reports of 15 additional cases were found after this article had been completed. Since it was impossible to include them in the detailed study, they have been added in an appendix. The total number of cases reported, therefore, is 105.

and reporting the case. Except for some seasickness, she had been well up to two days prior to landing, at which time she was taken with severe pain in the right side of the abdomen. She had fever, and was markedly prostrated. The right lower quadrant of the abdomen became very tender to pressure. On admission to the Hospital her temperature was 101°, and her pulse 100. The leukocytes were 23,000, and the polymorphonuclears 88 per cent. She had never been sick before, and there was no history of any pelvic disturbances. While evincing evidences of considerable prostration, at the same time she was very well nourished, and there was no sign of any cachexia. Physical examination showed the heart and lungs to be normal. The abdomen was distended and there were no respiratory abdominal movements. The whole right lower quadrant was rigid and very tender, both these signs shading off from a point of maximum intensity, situated at McBurney's point, where there was felt a mass the size of a lemon. Over this mass there was tympany, and there were no signs of free fluid in the abdomen. Rectal examination showed the pelvic organs to be normal, and no mass could be felt, but there was considerable tenderness high up in the right fornix.

Immediate operation was performed. An intermuscular incision, about two inches long, was made over the mass. On opening the peritoneum, the inserted finger pushed aside an adherent coil of intestine, which opened an abscess, well walled in, containing about 2 ounces of fœtid, thick, creamy pus. After sponging the cavity dry the appendix was found hanging over the brim of the pelvis, to whose walls it was adherent. On delivering it into the wound, it was seen to be about four inches long and as large as one's index finger. Its serosa was intensely congested, and about one inch from its base there was a gangrenous patch, in the centre of which there was a small perforation. Its tip was clubbed and hard, as though there was a concretion in its lumen. The meso-appendix was clamped in sections and divided. Two catgut ligatures were applied about its base, between which the appendix was amputated. The stump was cauterized by the Paquelin, after which a second plain catgut ligature was applied about the stump, which was followed by a second cauterization. The cavity was sponged out, and into it were inserted two small cigarette drains. The abdominal wall was sutured by layers, closely about the drains. The patient made an uneventful recovery, the wound being completely closed by the twenty-fifth day. The girl went home on the thirtieth day.

At the time of the operation there was no suspicion that the appendix, on external examination, was affected with anything more than an intense, acute suppurative inflammation. Owing to the lateness of the hour in the evening of the operation, the appendix was not cut open, but, following the ordinary routine, it was sent as it was removed to the pathologist, by whom a gross section of the

organ was made, and this revealed, macroscopically, that the tip, for half an inch, was occupied by a small fibrous appearing mass which completely filled the lumen. There was no concretion present. No suspicion of malignancy whatsoever was aroused at the time of the operation, as there was no tumor visible on the external surface, the tip being merely clubbed. No enlarged glands were seen in the meso-appendix.

The following is the report of the examination of the specimen by Dr. F. C. Wood, of the Pathological Department of Columbia University: The material consists of four transverse sections of

FIG. 1.—Carcinoma of the appendix (Case XXII), showing general distribution of the growth throughout the wall of the organ. (Low power.)

the appendix. Two of the fragments include a considerable portion of the meso-appendix. The other two are transverse sections of the free part of the organ. The appendix is considerably enlarged, measuring about 12 mm. in diameter after hardening. Two of the sections show merely a dilated appendix with no mucosa and a somewhat chronically inflamed peritoneum and subserous coats, the wall measuring 4 mm. in thickness. The other two specimens, which include the meso-appendix, show the following changes: The wall is thickened, measuring 6 mm. This thickening is chiefly in the submucosa and muscularis. At the periphery of the appendix and in the meso-appendix are a large number of leukocytes and blood. The leukocytes are chiefly polynuclear, many of them of the eosinophile group. The rest are lymphocytes and plasma cells.

The fat of the meso-appendix is infiltrated, and there is a formation of a considerable amount of new connective tissue in the form of granulation tissue. The bloodvessels are distended with blood. There is a thrombus in one of the larger veins. This more or less active inflammation extends entirely around the appendix, although in the portion opposite the mesenteric attachment the inflammation is much less than on the other side. The mucous membrane of this portion of the appendix is normal and the surface is unbroken. The submucosa, the muscularis, and the subserosa are infiltrated with cells arranged in large and small masses in the tissue spaces (Figs. 1, 2, and 3). These cells are polyhedral (Figs. 4 and 5); there is no connective tissue between the individual cells; the

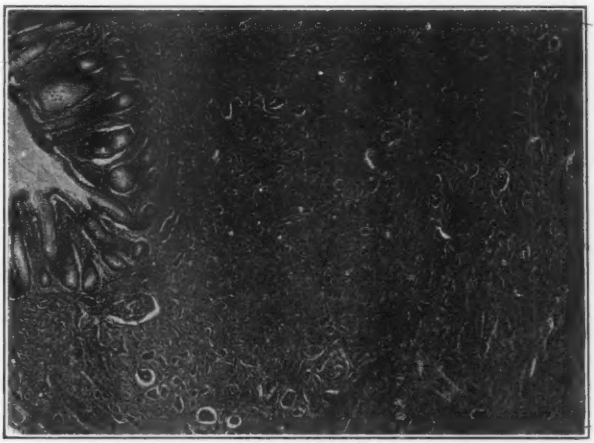

FIG. 2.—Carcinoma of the appendix (Case XXII), showing general distribution of the growth throughout the wall of the organ. (Medium power.)

nuclei are large and show well arranged chromatin network. Mitotic figures are scanty. None of the carcinomatous masses show any tendency to an alveolar formation, nor are there any high cylindrical or mucous cells. While the newgrowth extends up into the lymphoid tissue underneath the lining membrane of the lumen of the appendix, this epithelium is in no place broken through, nor in direct connection with the growth. The infiltrated tissue shows the usual evidences of chronic inflammation, and many wandering tissue cells of the type of plasmacytes and plasma cells are present in the muscle bundles near the newgrowth. The exact histogenesis of the tumor cannot be established from the specimen, as the entire appendix is not available for section; but the possibility of the tumor having arisen from the mucous membrane cannot

FIG. 3.—Carcinoma of the appendix (Case XXII), showing the topography of the growth beneath the mucosa. (Medium power.)

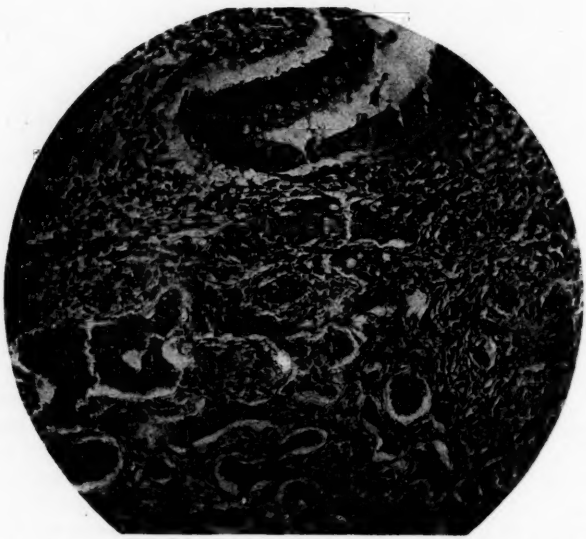

FIG. 4.—Carcinoma of the appendix (Case XXII), showing solid alveoli filled with polyhedral cells invading the submucosa. (High power.)

be excluded. The diagnosis is carcinoma of the appendix, polyhedral cell type; acute peri-appendicitis.

CASE XXVII.—Operator, Dr. A. J. McCosh. A male, aged twenty-five years, was admitted to the Presbyterian Hospital, New York, April 7, 1897. His difficulty began in the previous August, when he had sudden cramp-like pains in the right lower abdomen, accompanied by vomiting. No abdominal tenderness (?). The pains lasted two weeks. The next month, September, he had a similar attack, lasting three weeks. He was well until the following March (an interval of six months), when he was taken with sudden tenderness and pains in the right iliac fossa, abdominal distention, and vomiting. On admission, he was just recovering from this last

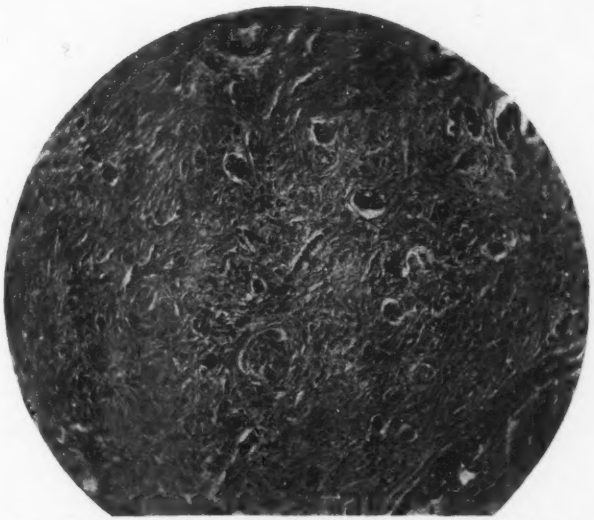

FIG. 5.—Carcinoma of the appendix (Case XXII), showing solid alveoli filled with polyhedral cells. (High power.)

attack. On examination there were rigidity and tenderness in the right iliac fossa. At the operation there was no fluid in the abdomen. There was felt a mass, 3½ inches in diameter and 1½ inches deep, with no pulsation in it. It was gradually mapped out, running obliquely behind the posterior peritoneum from the sacrum up to the right side. The appendix not seen. An aspirating needle introduced into the boggy tumor withdrew no pus. It was deemed a malignant mass, involving the cecum, appendix, and peritoneum. Removal was considered impossible, and the wound was closed. The patient was readmitted January 4, 1899, twenty months after his first operation. For the past eight months he has had attacks of cramp-

like pains in the region of the old scar, and these attacks are now recurring much more frequently. Has lost no flesh or strength; never jaundiced, and bowels regular. On examination, in old appendix wound, there is a ventral hernia. Palpating through this opening, there is found, at the usual site of the appendix, a hard mass, size of a walnut. Operation, January 10, 1899. Intestines and omentum matted together and covered with a serous exudate. Several large, hard masses felt in the posterior part of the abdomen, which proved to be retroperitoneal glands. The glands throughout the mesentery were enlarged and hard. Several of these were ex-

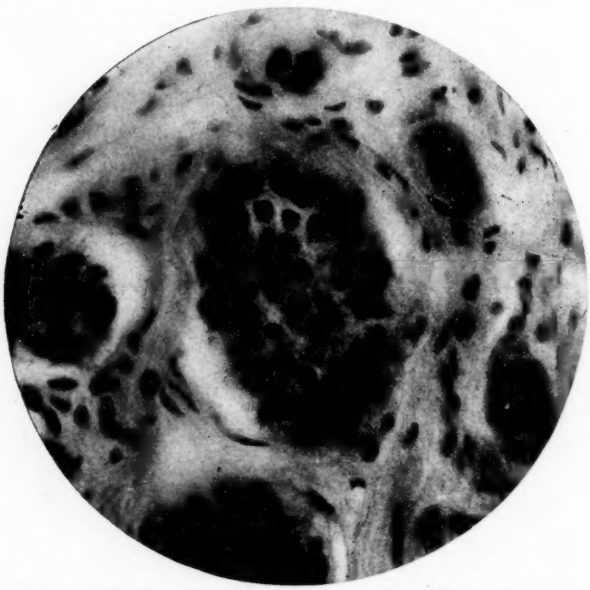

FIG. 6.—Spheroidal-cell carcinoma of the appendix (Case XXVII), showing alveoli filled with irregularly ovoid or polyhedral cells.

cised for examination. The appendix was separated from adherent intestines with much difficulty. It was short, thick, and gave evidences of chronic inflammation. The fluid from this region had a foul odor. Appendix removed. Incision closed with drainage.

Pathological number, 4239. October 1, 1899. Appendix and glands. In some parts of some sections there is a cancerous structure. Some alveoli are round and have a lumen, others are round and packed with cells, others are long and narrow, in places only a single row of cells. Some of the alveoli lie in smooth muscle. There is some inflammatory exudation at the surface of some portions. The lymph glands look normal. After-history: This patient was

seen in March, 1908, and was in perfect health. There is a symptomless ventral hernia in the scar but nothing abnormal is palpable in the iliac fossa. There has been, consequently, no recurrence after nine years.

Fortunately the slides were preserved. I submitted them to Dr. Wood, of Columbia University, on February 20, 1908, for the purpose of obtaining a photomicrograph, which is here reproduced (Fig. 6). His pathological report is as follows: The specimen consists of three mounted sections of a portion of the intestinal tract. From the thickness of the wall and the fact that there are four or five small gland tubules embedded in the lymphoid tissue, in one portion of one section, it is probable that the material was removed from the appendix. The muscular coats are arranged in a circular and longitudinal group, and scattered irregularly between the muscle bundles are alveoli filled with irregularly ovoid or polyhedral cells, with large nuclei containing well-marked chromatin. In other portions there is a diffuse infiltration of the muscle tissue with similar cells. At no place has the growth assumed an alveolar type. There are no mitoses visible in the cells. There is only very slight inflammatory reaction around the alveoli containing the cells of the newgrowth. There is no evidence of chronic inflammation of other portions of the tissue. The diagnosis is spheroidal-celled carcinoma of the appendix; whether primary in the appendix or not, it is impossible to say from the sections.[2]

CASE XXVI.—Operator Dr. J. Wiener. A male, aged thirty-five years, was admitted to Mt. Sinai Hospital, New York, December 8, 1903. As a child, inflammation of bowels. Five years ago, indigestion for six months with nausea and belching of gas, appetite fair, but with no pain. One year ago, nervous prostration, which kept him from work for six months. Moderate smoker, but not alcoholic. Eleven days before admission, sudden sharp, shooting pains in right lower quadrant. Next morning went to business, but about 11 A.M. felt nauseated, with chilly sensations and profuse sweating. Severe umbilical pains. A few hours later, temperature 103.6°. No vomiting. Bowels moved spontaneously. Went to bed and had fever and chilly sensations for three days, when the pain became localized in the right iliac fossa. Operation December 9, 1903, at which time nothing palpable in the right iliac fossa was felt, but there was slight tenderness on deep pressure in that region. Intermuscular incision. Many dense adhesions between cecum, parietal peritoneum, and ileum. Appendix firmly adherent below and internally to cecum. Separation of adhesions caused tearing of serosa of cecum in several places, which were repaired with silk sutures. Appendix two inches long, very narrow, especially at base;

[2] That it was primary in the appendix is proved by the material removed at the operation and by the non-recurrence after nine years.

near its tip and projecting into the meso-appendix was what was taken to be a small gland. In the mesentery, near the ileocecal junction, a large gland was found and removed. This gland, together with the tip of the appendix was submitted to the pathologist, Dr. Mandlebaum. Out of bed on the tenth day, and the wound healed in two weeks. The diagnosis is adenocarcinoma near tip of the appendix; obliterating appendicitis; hyperplasia of mesenteric gland. The patient was well four years later, that is, at the present time.

In connection with these cases, I have gone over the literature and have collected all the reported cases of primary carcinoma of the appendix that I could find after an exhaustive search. In 1906 Rolleston and Jones published a report of 42 cases of malignant tumors primary in the appendix, all doubtful cases having been excluded. Since Rolleston's paper, no collection of such cases has appeared in English. I have found 48 cases in all, which, in addition to those of Rolleston, make a total of 90 undoubted cases. No case in which the tumor has been found involving the cecum, even to the slightest degree, has been included in either series, because in such cases it is impossible to say where the cancer originated, whether in the cecum or in the appendix.

The following is a list of 48 cases. The number before each case refers to the corresponding references throughout this article:

I. Landau. Berl. klin. Woch., December 10, 1906.
II. Villar. Gaz. hebdom. des Soc. méd. de Bordeaux, January 3, 1904, p. 3.
III. Weinberg. Bull. et mém. de la Soc. anat. de Paris, 1905, No. 3, p. 38.
IV. Baldauf. Albany Medical Annals, December, 1905.
V. Baldauf. Ibid.
VI. Baldauf. Ibid.
VII. Warthin. Physician and Surgeon, Detroit, December, 1906, p. 544.
VIII. Eccles. Amer. Jour. Med. Sci., June, 1906, p. 966.
IX. Fauldner. Lancet, 1906, i, 598.
X. Brandts. Münch. med. Woch., 1907, September 3, p. 1780.
XI. Brandts. Ibid.
XII. Driessen. Beiträge zur klin. Chir., 1907, liv, 252.
XIII. Lejars. Bull. et mém. de la Soc. de Chir. de Paris, March 12, 1907.
XIV. Zaaijer. Beiträge zur klin. Chir., liv, 308 (No. 1 of his cases).
XV. Zaaijer. Ibid. (No. 2 of his cases).
XVI. Zaaijer. Ibid. (No. 3 of his cases).
XVII. Zaaijer. Ibid. (No. 4 of his cases).
XVIII. Kaufmann. Spec. patholog. Anat., 1904, 3d edition, p. 464. Case 1.
XIX. Kaufmann. Ibid. Case 2.
XX. Jong. Mitt. aus d. Grenzg. der Med. und Chir., 1907, xviii, Nr. 3.
XXI. Hessberg. Carcinoma Processus Vermiformis, Inaug. Diss., München, 1904.
XXII. McWilliams. This article, p. 822.
XXIII. Zaaijer. Same reference as Cases 14, 15, 16, 17 (his Case No. 5).
XXIV. Zaaijer. Ibid. (his Case No. 6).
XXV. Zaaijer. Ibid. (his Case No. 7).
XXVI. Wiener. This article. Not previously published, p. 829.
XXVII. McCosh. Ibid, p. 827.
XXVIII. Barrow. Georgia Practician, February 15, 1905.
XXIX. Pauchet. Gazette médicale de Picardie, 1900, xviii, 146.
XXX. Nélaton. Bull. et mém. de Soc. de chir. de Paris, March 12, 1907, p. 228
XXXI. Hartmann. Ibid., March 5, 1907, Case 1.
XXXII. Hartmann. Ibid., Case 2.

XXXIII. Mason and Rhea. Boston Med. and Surg. Jour., January 10, 1907, p. 44.
XXXIV. Grunbaum. Berl. klin. Woch., August 5, 1907, Nr. 31, p. 984.
XXXV. Patel. Lyon médical, 1907, cix, 276.
XXXVI. Cullingworth and Corner. Lancet, 1904, ii, 1340.
XXXVII. Neri. Beiträge zur path. Anat., 1905, xxxvii, 163.
XXXVIII. de Bovis. Revue de Chir., 1900, p. 708.
XXXIX. Deaver. Amer. Jour. Med. Sci., 1906, p. 845.
XL. Deaver. Ibid.
XLI. Becker. Münch. med. Woch., July 10, 1906, Nr. 28, p. 1383.
XLII. Grieg. Lancet, 1907, ii, 1466.
XLIII. Mandlebaum. Proc. New York Path Soc., 1905.
XLIV. Mandlebaum. Ibid.
XLV. Korte. Verhand. der Deut. Gesell. f. Chir., 1905, xxxiv.
XLVI. Korte. Ibid.
XLVII. Korte. Ibid.
XLVIII. Libmann. Proc. New York Path. Soc., 1906, No. 6.

I have excluded the following cases because they have either not seemed to be positively cancerous appendices or else not undoubtedly primary in the appendix:

De Ruyter. Archiv. f. klin. Chir., Band lxix, p. 281.
Edington. Glasgow Med. Jour., I, 120.
Meyerstein. Carcinoma Append. Vermiformis, Inaug. Diss., München, 1905.
Martin. Trans. South. Med. and Surg. Assoc., xvii.
Westerman. Beiträge zur klin. Chir., 1907, liv, 258.
Sudsuki. Three cases of "lymphangitis plastica," Mitt. aus den Grenzg. der Med. und Chir. 1901, vii, 516.

The results of the study of these 48 cases are given in the following pages. In many instances they will be found combined with the statistics of Rolleston, in order that certain facts may be more authoritatively established. In no region of the body are we able to obtain cancers in such an early stage of their development as those occurring primarily in the vermiform appendix, and their careful study should in future elicit new and important information with regard to many points in the life history of malignant neoplasms. Consequently, every case should be accurately observed and reported. Now that attention has been drawn to its occurrence so frequently, it can no longer be considered a curiosity.

Reasons which Led to the Removal of the Appendix. Of the 48 cases in this series, details are wanting as to this point in 3. Of the 45 remaining cases, 2 appendices were removed at autopsies for other conditions, namely, Case XVIII (Kaufmann), in which the distally enlarged appendix was removed from the body of woman, aged thirty-one years, who had died in the fourth week of typhoid; and second, Case XXI (Hessberg), in which the primary cancer was found in the appendix of a woman, aged seventy-six years, who had died of general miliary tuberculosis and arteriosclerosis; 36 of the remaining 43 patients suffered from some variety of appendicitis. In Rolleston's series of 33 patients who were operated upon, 27 had symptoms pointing to appendicitis in some form. Thus, out of a total of 76 patients operated upon, 63 (83 per cent.) had had such symptoms. Following the latter's classification, I shall divide these as follows:

1. Symptoms of the first acute attack, operation during or immediately after the first acute attack:
   McWilliams, 13 (Cases 4, 6, 22, 24, 26, 29, 30, 31, 34, 45, 47, 48, 49).
   Rolleston, 10
   Total, 23, or 36.5 per cent.
2. Chronic symptoms without acute attack:
   McWilliams, 8 (Cases 15, 16, 17, 19, 20, 36, 37, 42).
   Rolleston, 5
   Total, 13
3. Chronic with one or more acute attacks:
   McWilliams, 2 (Cases 14, 25).
   Rolleston, 3
   Total, 5
4. Recurrent attacks:
   McWilliams:
   Two attacks, 5 (Cases 3, 10, 13, 23, 28).
   Three attacks, 5 (Cases 5, 8, 9, 12, 44).
   Five attacks, 3 (Cases 2, 32, 27).
   Total, 13
   Rolleston, 9
   Total, 22

From these figures we find that of the 63 patients with some variety of appendicitis, 23 (36.5 per cent.) had their appendices removed during or immediately after the first acute attack. In these cases it would seem more than likely that the growth was the cause of the acute inflammations, acting in a manner similar to a concretion. For the growth may occlude the lumen, causing stagnation of material beyond the tumor, with the resulting changes in the mucous membrane, allowing the entrance of micro-organisms, or the same condition may be brought about by ulceration of the surface of the tumor, o. its breaking down through lack of nutrition, due to obliteration or compression of the bloodvessels. The question then immediately comes up, What causes the growth itself? This will be discussed later.

Forty patients, or 63.5 per cent., had had symptoms of chronic appendicitis in some form for varying periods of time. Of these, 17 are to be found in Rolleston's series, and 23 in my own. I have been able from the imperfect records to ascertain the duration of the symptoms in the following cases:

12 years,	2 cases,	Jones and Simmons, Zaaijer.
7 "	2 "	Weinberg, Kelly and Hurdon.
5 "	1 "	Neri.
4 "	2 "	Hartmann, Jong.
3 "	4 "	Moschkowitz, Driessen, Zaaijer, Villar.
2 "	5 "	Weir, Burnham, Kaufmann, Zaaijer, Mandlebaum, McCosh.
1 "	4 "	Battle, Barrow, Deaver, Eccles.
Many yrs.,	1 "	Kaufmann.
9 months,	1 "	Landau.
7 "	1 "	Baldauf.
3 "	2 "	Lejars, Zaaijer.
2 "	1 "	Cullingworth and Corner.
	26 cases.	

These figures show that symptoms existed for over a year in 21 patients (more than 28 per cent.). This lends weight to the theory that chronic inflammatory changes are the cause of malignancy.

It would be interesting to inquire, then, in this connection, how many of these appendices, removed from patients with chronic symptoms associated with cancer, showed the microscopical lesions of chronic inflammation? There were 23 patients in my series with chronic symptoms, and associated chronic lesions were found by the microscope in the following cases: Baldauf (V), Eccles (VIII), Brandts (X), Driessen (XII), Zaaijer (XIV), Zaaijer (XV), Zaaijer (XVII), Zaaijer (XXV), Deaver (XXXIX), Hartmann (XXXII), Neri (XXXVII), Barrow (XXVIII), Weinberg (III), Mandlebaum (XLIV), Hessberg (XXI), Zaaijer (XXIII), McCosh (XXVII).

Thus, out of 23 cancerous appendices removed for chronic symptoms, in 16 (70 per cent.) it is definitely stated that chronic inflammatory lesions were present in addition to the cancers. In the remaining 7 of the 23 cases, the descriptions of the microscopic findings were either too meagre or too indefinite to judge as to this point.

Are we able to find with the microscope chronic lesions in the cancerous appendices removed from patients in the first acute attack? In my own series of 13 acute cases, I found with regard to this question the following to be the facts:

Case	IV. Baldauf.	Chronic lesions were stated to be present.
"	VI. Baldauf.	" " " "
"	XXII. McWilliams.	" " " "
"	XXIV. Zaaijer.	" " " "
"	XXIX. Pauchet.	Not mentioned in record.
"	XXXI. Hartmann.	" " "
"	XXXIV. Grunbaum.	" " "
"	XLVII. Korte.	" " "
"	XLVIII. Korte.	" " "
"	XLIX. Libman.	Chronic lesions present.
"	XLV. Mandlebaum.	" " "
"	XXX. Nélaton.	" " "
"	XXVI. Wiener.	" " "

Of these 13 cases, in which cancers were found in appendices removed in the first acute attack, there are 8 (61 per cent.) in which mention is made of chronic inflammatory lesions being found in addition to the cancers.

In 7 of the 48 cases the primary cancerous appendix was removed in the course of other operations:

Case I. Landau. Myomectomy; left salpingoöphorectomy; appendix removed because of bulbous tip. Chronic lesions also present. Female, aged thirty-three years.

Case VII. Warthin. Acute pelvic abscess, due to pyosalpinx; right salpingoöphorectomy; appendix removed because irregularly

thickened. Chronic lesions found with the microscope. Female, aged thirty-two years.

Case XI. Brandts. Symptoms before operation thought to be due to biliary calculi, because of jaundice and recurring pains. Cholecystectomy. Appendix clubbed. Chronic lesions present in appendix. The author says that the "attacks were due to chronic appendicitis caused by the cancer." Male, aged thirty-five years.

Case XX. Jong. Patient had diarrhœal attacks for four years, which were referred to a chronic appendicitis. Removal of the appendix cured the attacks. Appendix found to have a very thick proximal mucous membrane and a stenosis, 2.5 cm. from the tip, which caused a cyst in tip with thick walls. In the appendix, chronic lesions found generally and a cancer in the cyst. Female, aged forty-seven years.

Case XXXIII. Mason and Rhea. In 1903, cyst of ovary removed. In 1905, resection of the tube and ovary for cyst and hydrosalpinx. In 1906, operation for subacute pelvic pains, curettage, ventrosuspension, resection of ovary, and removal of normally appearing appendix, "to prevent any possible further trouble." Chronic lesions present, as well as a small cancer in the tip, only visible by means of the microscope. Female, aged twenty years.

Case XXXV. Patel. Operation for double inguinal herniæ. The right one was tender and irreducible, and contained an adherent appendix. No mention in the record of any lesion except the cancer. Male, aged fifty-eight years.

Case XXXVI. Cullingworth and Corner. Fibromyoma of uterus removed. Appendix amputated because of bulbous tip. Chronic lesions also present. Female, aged thirty-one years.

In these 7 cases the cancerous appendices were chance findings. The average age of these patients was 36.5 years. Rolleston gives 4 such patients, all operated upon for pelvic lesions.

Summarizing, then, the presence or absence of chronic lesions in my series of 48 cases, I find the following to be the facts:

Among the 23 patients operated upon for chronic appendicitis, 16 were stated to have chronic lesions present, as found by the microscope. Of the 13 patients operated upon for acute appendicitis, 8 were definitely stated also to have chronic lesions present. In 6 of the 7 patients from whom the appendices were removed in the course of other operations, chronic lesions were found. Thus, there was a total of 30 patients out of 48, or 62 per cent., in whose cancerous appendices associated chronic lesions were found by the microscope. Which is primary, the chronic inflammation or the cancer? As yet, there is no correct answer to this question apparently. We may summarize, then, the reasons for the discoveries of the cancers as follows:

	McWilliams.	*Rolleston.*	*Totals.*
Acute appendicitis	13	10	23
Chronic appendicitis	23	17	40
Appendices removed in the course of pelvic operations	4	4	8
Iliac fistulæ	0	2	2
Inguinal hernia	1 (Case 35)	0	1
Appendectomy and cholecystectomy	1 (Case 11)	0	1
Appendectomy for chronic diarrhœa	1 (Case 20)	0	1
Autopsies	2	8	10
Unknown	3	1	4
Totals	48	42	90

FREQUENCY OF OCCURRENCE OF PRIMARY CARCINOMA OF THE APPENDIX. This is difficult to ascertain statistically, because in most of the published reports of series of cases, in which the appendices were removed for some reason or another, there is not given the number of appendices which were examined systematically by the microscope; only such cases ought to be included in figures designed to show the relative frequency of primary cancers in removed appendices, because in a large number of cases in my series the tumors were not found except when sections had been examined under the microscope. Many of the appendices containing the cancers were considered at the time of the operations, when viewed macroscopically, to be tuberculous or to be merely the seat of simple cicatrices. The following are reported series of cases with the number of cancerous appendices in each; it is not mentioned in reports just how many of the appendices were examined microscopically:

Baldauf	6 cancers in	735 appendices.
Neri	1 cancer in	82 "
Elting	2 cancers in	320 "
Jong	1 cancer in	255 "
Schrumpf	1 cancer in	150 "
Moschkowitz	6 cancers in	2000 cases.
Zaaijer	4 cancers in	463 "
Kelly (Deaver's cases)	5 cancers in	2500 appendices.[3]
Total	26 cancers in	6505 appendices, or 0.4 per cent.

This frequency of cancer of the appendix differs radically from the conclusions of Baldauf and of Zaaijer, who maintain that such tumors occur in 1 per cent. of the cases of appendicitis. Their figures are based, however, on a much smaller number of cases than are mine. From my series above, this percentage of Baldauf is altogether too large. It is impossible to judge from the tabulated reports of the above-mentioned authors in what proportion of the cases microscopic examination of the appendices was made. Had such been made in all cases, it is not to be questioned that additional

[3] Personal communication from Dr. A. O. J. Kelly. Microscopic examinations were made of all these 2500 appendices. Not included are two cases of endothelioma.

carcinomas would have been found. Until a large number of appendices are examined critically with the microscope, it will be impossible to ascertain correctly just what the true frequency of primary cancer of the appendix is. It is more than likely that many of the cases of cancer of the cecum are due to secondary extensions from a primary growth in the appendix. I have not included any such cases in my statistics.

AGE. In 42 of my series of 48 cases the ages are known, and are as follows:

	McWilliams.	*Rolleston.*	*Total.*	*Per cent.*
Between 1 and 10 years	2 cases	0	2	3
" 10 " 20 "	9 "	7	16	20
" 20 " 30 "	16 "	13	29	37
" 30 " 40 "	10 "	7	17	22
" 40 " 50 "	1 case	5	6	8
" 50 " 60 "	1 "	2	3	4
" 60 " 70 "	1 "	1	2	3
" 70 " 80 "	1 "	0	1	1
" 80 " 90 "	..	1	1	1
Total	42 cases	36	78	99

Average age 27.7 years.

There were 2 patients aged eight years (Cases VI and X), 1 aged twelve (Case XXIV), 1 aged fifteen (Case XLIX). The oldest patient in my series was aged seventy-six years. It will thus be seen that 27 of the 42 cases, or 66 per cent., of primary cancer of the appendix in my series occurred before the age of thirty. The combined statistics of Rolleston and mine give 47 out of 78 cases, or 60 per cent., as occurring before thirty. The average age in the combined statistics is twenty-nine years.

This is in striking contrast to the age incidence in malignant tumors of the remainder of the intestinal canal. Thus, Rolleston gives, in 41 cases of primary cancers of the duodenum, the average age as fifty-two years; in 9 cases of primary carcinoma of the jejunum and ileum it was 47.2 years; in 30 cases of primary carcinoma of the cecum, 47.8 years; and in 100 cases of primary carcinoma of the remainder of the large intestine, 49.34 years. Thus, we find in 180 cases of cancers of the intestinal canal, exclusive of the appendix, the average age is forty-nine years; while in 77 cases of primary cancers of the appendix the average age is twenty-nine years, which shows that the average age incidence in primary cancer of the appendix is twenty years less than in other parts of the intestine.

Mandlebaum reports that among 96 cases of primary cancer of the intestine occurring in the Mt. Sinai Hospital, New York, 5 were primary in the appendix, or 5.2 per cent. These cases constituted 0.75 per cent. of cancers from all sources. These are undoubtedly very high percentages of frequency, and cannot be accepted as generally typical.

From these statistics it seems that the age incidence of primary

cancer of the appendix corresponds somewhat closely to that of simple appendicitis. Thus, Deaver, in 3000 cases of ordinary appendicitis, found the following to be the age percentages (I add the percentages in the cancer cases as contrast):

	Simple appendicitis.	*Cancer of appendix.*
From 10 to 20 years	27.5 } or 69 p. c.	23.0 } or 60 p. c.
" 21 to 30 "	41.5 } before 30	37.1 } before 30
" 31 to 40 "	20.1	21.8
" 41 to 50 "	7.0	7.6
" 51 to 60 "	2.8	3.8
" 61 to 70 "	0.6	2.5
" 70 to 80 "	..	1.2
" 80 to 90 "	..	1.2

SEX. These were divided as follows:

	McWilliams.	*Rolleston.*	*Total.*	*Per cent.*
Females	24	20	44	57.1
Males	17	16	33	42.8

From these figures it appears that the disease occurs more frequently in women than in men, the difference in frequency being 15 per cent. in favor of the female sex. It has been suggested that this may be due to the more frequent performance of laparotomy in women than in men. In addition, the proximity of the appendix to the female generative organs, with the possibility of extension to the appendix of irritation induced by inflammation of these organs, may have something to do with its greater frequency among women. Thus, in the 7 cases in my series in which cancerous appendices were removed in the course of other operations, 5 of these occurred in women, 4 of whom were operated upon for pelvic conditions. In Rolleston's 6 cases, operated upon for conditions other than appendicitis, 4 were for pelvic lesions. In a total, then, in Rolleston's and my own series of 13 operations, in course of which the appendices were removed, 8 were upon the female pelvic organs. This brings up the moot question, whether it would not be the part of wisdom in all cases to remove the appendix when one is operating in its vicinity.

Deaver found, in 3000 cases of ordinary simple inflammations of the appendix, that 62 per cent. occurred in men and 38 per cent. in women. Many authorities maintain that ordinary inflammation in the appendix is the exciting cause of the development of primary cancers in them. If such ordinary inflammations occur in 62 per cent. of the cases in men and 38 per cent. in women, we should naturally expect that these primary cancers of the appendix would be more frequent in men; but the very reverse is the case, for 57 per cent. of primary cancers of the appendix occur in women and 42 per cent. in men. What is the reason for this reversal of frequency in the two sexes in the two affections? At present there seems to be no explanation whatsoever that adequately answers

this question; we must simply accept it as a fact, to be confirmed or rejected, as the case may be, later by a larger number of cases.

CONCRETIONS. These were mentioned as being present in only 2 cases (X and XXXV). Rolleston found in his series of 42 cases that calculi were present in 3 cases. This makes a total of 5 cases out of 90, or 5.5 per cent. From this we may infer that concretions form a very small role, if any, in the etiology of cancers of the appendix, which is in striking contrast to the frequency with which calculi in the gall-bladder are found associated with primary cancer in that organ.

In only 1 recorded case of primary cancer of the appendix is there mention of a foreign body (other than coprolith) having been found. This is Case XXXV (Patel), in which a cancer and a small fish-bone were found in an appendix in an inguinal hernia.

The great rarity (5 per cent.) of fecal concretions in appendices containing primary cancers is in striking contrast to the frequency with which these bodies (not including other foreign bodies) are met with in operations for the removal of the appendix for ordinary inflammatory conditions. Thus, I have collected the following statistics with regard to the frequency of fecal concretions in ordinary appendicitis:

	Cases.	*Fecal concretions.*
Fitz	300	15
Ranvier	459	179
Murphy	141	43
Deaver	460	74
Schuylenburch	271	36
Hawkes	66	8
Hagen	184	21
Nordman (Korte)	1522	608
Total	3403	984¼ (or 28.2 per cent.)

ENLARGED GLANDS. These were mentioned as being present at the time of the operation in only 5 of the cases in my series, or 10 per cent., namely, Cases I (Landau), VIII (Eccles), XXVIII (Barrow), XXVI (Wiener), XXVII (McCosh).

In Eccles' case there were two small glands in the meso-appendix, which, unfortunately, were not examined microscopically. The later history of this patient is not given. In Barrow's case the mesentery of the ileum, cecum, and part of the ascending colon contained ten or more, both palpably and visibly enlarged glands, one or two of them being as large as an adult thumb. They were deemed tuberculous at the time of the operation, being considered, erroneously, secondary to tuberculosis of the appendix. There was no microscopic examination of these glands. This patient is well at the present time, four years after the operation. In Landau's case the meso-appendix contained one pea-sized gland, which, on microscopic examination, was found to be free from cancer. The

later history of this patient is not given. In Wiener's case (XXVI) a large gland was removed from the mesentery near the ileocecal junction. Microscopic examination showed that it was free from cancer and was merely hyperplastic. This patient was well four years after the operation. In McCosh's case (XXVII), there were many large glands present, but the microscope proved these to be uninvolved by cancer. This patient was perfectly well nine years after the appendectomy.

In 2 cases in my series, Hartmann (XXXI), Baldauf (IV), there were small masses in the meso-appendix which at the time of the operations were considered to be enlarged glands, but which later, on microscopic examination, were found to be metastatic cancerous masses, secondary to the cancers in the appendices, and were not cancerous glands.

In Rolleston's series of cases there were 3 patients in whom the abdominal lymphatic glands were enlarged (the cases of Fiske-Jones and Simmons, Beger, and A. O. J. Kelly). In the case of Fiske-Jones and Simmons, it was found by the microscope that the enlarged mesenteric glands were unaffected with cancer. The patient was well seven months after the operation. Beger's case did not survive the attempt to remove an iliac sinus, due to a cancerous appendix, which had existed for three and a half years. The fistula was found to lead directly into the appendix, which was infiltrated throughout by carcinoma, the growth projecting into the cavity of the cecum, but not actually involving its walls. On post-mortem examination, the retroperitoneal glands were found to have become implicated, but there was no suggestion that the growth in the appendix was other than primary. In the case of A. O. J. Kelly, the peritoneum was studded with very small grayish nodules which suggested miliary tubercles. The patient died on the sixth day as the result of an operation to replace protruding intestines. At the time of the primary operation the retroperitoneal glands were found enlarged (apparently these were not examined microscopically).

Thus, out of 90 cases, only 8 had enlarged glands, or 9 per cent. Of these, in 4 cases the microscope showed that the enlarged glands were not implicated with cancer. In 3 cases the enlarged glands were not examined microscopically. In only one case (1 per cent.) was it positively demonstrated that the glands were cancerous. Hence we must infer that these cancers of the appendix are exceedingly slow in involving the lymphatics. As will be shown later, however, they do spread into the meso-appendix by direct continuity.

Situation of the Tumors. In 38 of the 48 cases in my series this is found to be as follows (10 of the records are defective in this regard); Rolleston's series of 33 cases is also added:

	McWilliams.	*Rolleston.*	*Total.*	*Per cent.*
At or near the tip	26	16	42	59.15
In the middle	6	4	10	14.08
Near the base	2	8	10	14.08
At the middle and tip	1	1	2	2.81
Near the base and middle	1	0	1	1.40
Almost the whole appendix	2	4	6	8.44
Total	38	33	71	

From these figures we find that in over 59 per cent. of the cases the tumors were situated at or near the tip, and in 76 per cent. they were located at or distal to the middle. These are striking facts, since it indicates that primary cancers of the appendix develop in the regions where strictures, obliterations of the tip, and chronic inflammatory tissues occur most commonly. One can consequently scarcely refrain from arguing that there may be an etiological connection between these processes and the tumors. Such a relationship is further suggested by finding with the microscope that these cancers often develop directly in these pathological tissues, from which we may possibly infer that the cancer is a new implantation on a prepared ground. These regions, the seats of predilection for cancers, are likewise most exposed to nutritional changes, due to malpositions and twistings, all of which conduce to decadence of tissues.

When all is said that can be said in favor of the view that the chronic inflammation is the precursor and cause of the development of the cancers, no one can deny that the reverse may be true, namely, that the cancer causes the chronic inflammatory changes. To this latter view, it may be objected that the chronic symptoms have, in many of the instances, existed for so long a period of time, years in some of the cases, as to make the existence of cancer for so long a period improbable. This objection, however, may be met by the statement that these primary cancers of the appendix are more than likely of very slow growth, particularly in the beginning. At present we are not in the position of being able to state positively which is primary, the cancer or the chronic changes in the appendix.

Macroscopic Appearances of the Appendices. Information is afforded by a perusal of the records as to this point in 42 cases. The analysis shows some interesting results:

1. No tumor was present to the naked eye in 14 cases (33.3 per cent.) of the 42 cases. These were Cases 3, 4, 5, 6, 7, 9, 13, 15, 18, 19, 33, 37, 42, 43.

2. A cyst was present in 3 cases (0.7 per cent.); size (*a*) small, No. 20; (*b*) bean, No. 1; (*c*) large, No. 29 (4 inches long by $2\frac{2}{5}$ wide, with a twisted pedicle).

3. One or more solid tumors were present in 23 cases (55 per cent.). (*a*) Single tumor, 19 cases: size (1) small, 4 cases, Nos. 24, 25, 36, 39; (2) pea, 13 cases, Nos. 2, 10, 12, 14, 16, 21, 22, 23, 26,

30, 31, 44, 49; (3) bean, 2 cases, Nos. 17, 45. (*b*) Two tumors, 3 cases, Nos. 8, 28, 32. (*c*) Numerous tumors, 1 case, No. 35.

4. Clubbed tip only, 2 cases, Nos. 11 and 34.

5. In 9 cases, there were found obliterated areas ("cicatrices"), which later under the microscope were discovered to be cancerous cicatrices. These were Cases 3, 5, 7, 14, 21, 25, 33, 36, 37.

6. In 2 cases ulcers were present, Nos. 4 and 6. In both of these cases cancers were found in the ulcers themselves.

7. Perforations were present in 2 cases, Nos. 10 and 22, and concretions were found in 2 cases, Nos. 10 and 35.

8. Four of the cases, all of which had visible small tumors, were thought at the time of the operation to have tuberculous appendices. These were Cases 8, 10, 28, 31. The microscope alone revealed their true nature.

This analysis is interesting to the operating surgeon, for in only 55 per cent. of the cases were visible tumors present. Many of these tumors, however, could not be seen from the outside, as the growths often projected into the lumen without any external prominences, as was instanced in my own case (XXII). In 14, or 33 per cent., no tumors were visible to the naked eye, even after the appendices had been opened throughout. Three of the appendices, before they were cut open, were erroneously thought to have diverticula as the cause of the prominences at the time of the operations.

From these statistics, then, it is easily seen how fallacious it is to argue that because there is no visible tumor there can be no cancer present; only by careful microscopic examination can possibility of cancer be excluded. Hence the inaccuracy of any statistics based solely on the macroscopic appearances alone of the appendices.

PATHOLOGICAL CLASSIFICATION OF THE TUMORS. This is a somewhat difficult task, by reason of the different aspects in which this part of the theme has been considered, and on account of the use of a widely varying nomenclature by the authors. I have been assisted in this division by Dr. F. C. Wood, of the Pathological Department of Columbia University, New York, to whom my thanks are due for the assistance, as well as for the photomicrographs which accompany this article.

The following divisions of the neoplasms have been made, based on the microscopic examinations. There are 71 cases in which such examinations are reported:

1. *Columnar-cell Tumors.* Among these I have also included those which in the records are called adenocancers, cylindrical-cell cancers, and alveolar cancers. There were 14 of this type, or 33 per cent. of the 42 cases in which the variety of cancer was stated in my series of 48 cases. These were Cases 2, 3, 12, 21, 26, 29, 30, 31, 32, 37, 43, 46, 47, 48. The age and sex are stated in 11 cases:

6 females, average age 39.5 years. 1 was 76 and another 63.
5 males, " " 30.5 " 2 were 35.

11 average age 35 years.

2. *Spheroidal-cell Cancers.* Among these are included scirrhus cancers, solid globocellular cancers, basal-cell cancers, cancer simplex, polyhedral-cell cancers, carcinoma solidum diffusum, polymorphous-cell, and round-cell cancers. Of these there were 22 cases, or 52.4 per cent. of the 42 cases in my series, in which the variety of neoplasm is stated.

15 females, average age 23.6 years.
7 males, " " 23.4 "

22 average age 23 years.

These cases were Nos. 1, 4, 5, 6, 7, 8, 10, 13, 15, 18, 19, 20, 22, 24, 25, 27, 33, 34, 36, 44, 45, 49.

3. *Mixed Types.* Four cases, 1 male, 3 females; average age 29.7 years. (*a*) Scirrhus cancer with intimation of adenocancer, No. 11, male, aged thirty-five years. (*b*) Cancer solidum alveolare, partim solidum diffusum, No. 14, female, aged thirty-five years. (*c*) Partly adenocancer, partly cylindrocellulare solidum, partly carcinoma solidum diffusum, No. 16, female, aged twenty-six years. (*d*) Partly adenomatous, chiefly solid and diffuse, No. 23, female, aged twenty-three years.

4. *Columnar-cell cancer* undergoing spheroidal-cell transformation, 1 case, No. 9, age and sex not given.

5. *Colloid Cancer.* Case No. 17, male, aged twenty-five years.

6. *Endothelioma.* None in my series.

7. "*Cancer*" the only designation. Cases 28, 35, 39, 40, 41, 42. Total, 6 cases. In only 3 of these 6 cases are the ages and sex given. There were 2 males with an average age of thirty-eight years and 1 female of seventeen years.

COMBINED STATISTICS.

	McWilliams.	*Rolleston.*	*Totals.*	*Per cent.*	*Average age.*
Columnar-cell cancers	11	5	16	22.5	43.5
Spheroidal-cell cancers	22	16	38	53.5	23.5
Transitional cancers	1	6	7	9.8	32.7
Mixed cancers	4	0	4	5.6	29.7
Colloid cancers	1	2	3	4.2	
Endotheliomas	0	3	3	4.2	
Total	39	32	71		32.3

From these statistics we see that the spheroidal-cell cancers are 30 per cent. more frequent than the columnar-cell types. There is also a difference of twenty years in the average age incidence in the two varieties of cancer, the average age in the spheroidal-cell cancers being twenty-three years and in the columnar-cell type forty-three years.

If we compare the frequency of these various types of cancer in the remaining portions of the alimentary canal, we find the following to be the case in this regard:

Petersen and Colmers:
Large intestine:

	Per cent.
Adenocancer	86.5
Spheroidal cell	13.5

Kappers and Van Rooyen:
Stomach and intestines:

	Per cent.
Adenocancer	56.6
Mixed forms	13.2
Spheroidal cell	20.7
Colloid	9.5
Intestines alone:	
Adeno-cancer	72.7

If we compare these figures with those showing the frequency of the different types in appendical cancers, we have a striking contrast.

	Stomach with intestines. *Per cent.*	*Large intestine.* *Per cent.*	*Intestines alone.* *Per cent.*	*Appendical cancers.* *Per cent.*
Adenocancers	56.6	86.5	72.7	22.5
Spheroidal-cell cancers	20.7	13.5	..	53.5
Colloid cancers	9.5	..	..	4.2
Mixed cancers	13.2	..	..	5.6

Hence we see that in the appendical cancers, the columnar-cell or adenomatous cancers occur in about one-quarter of the cases only, while in the direct intestinal tract this type of cancer is the rule, occurring in almost three-quarters of the patients. In the stomach and intestines taken together, the spheroidal-cell cancer is found in only one-fifth of the cases, while in the appendix this type of cancer is found in over one-half of the cases. Colloid cancers of the appendix seem to be rarer than in the other portions of the intestinal tract.

What the significance of these observations is I do not pretend to be able to state or even to speculate about.

A rather striking similarity between the frequency of the occurrence of the various forms of the stomach and appendical cancers is shown when we compare the statistics on this point of 115 cases of stomach cancer reported by Fenwick and the 71 cases of appendical cancers in my series:

	Stomach cancer. *Per cent.*	*Appendical cancer.* *Per cent.*
Columnar-cell	28.6	22.5
Spheroidal-cell	63.3	53.5
Colloid cancer	7.8	4.2

MICROSCOPIC EXTENT OF THE GROWTHS. Of the 48 cases in my series, there are records regarding this point in 31 cases, as follows: The neoplasm extended through the mucosa and submucosa

alone in 4 cases, or 12.7 per cent., Cases 6, 12, 30, 37. Through the mucosa, submucosa, and muscularis only in 8 cases, or 25.8 per cent., Cases 10, 14, 15, 18, 22, 24, 29, 32. Through the mucosa, submucosa, muscularis, and subserosa in 4 cases, or 12.7 per cent., Cases 5, 11, 17, 33. Through all coats without involvement of the meso-appendix in 8 cases, or 25.8 per cent., Cases 1, 7, 19, 20, 21, 25, 27, 34. Through all the coats with involvement of the meso-appendix in 7 cases, or 22.5 per cent., Cases 3, 4, 13, 16, 23, 28, 31.

From these statistics, then, we find that these appendical neoplasms, when viewed histologically, have a malignant character, showing a tendency to infiltrate progressively contiguous structures (15 cases out of 31, or 48.4 per cent., involving all the coats of the appendices), but without, however, evincing evidences of producing distant metastases or of affecting neighboring lymphatic glands. This invading characteristic is evidently of slow progress, fortunately for the patients. This slow growth is further evidenced by the scarcity of mitotic figures in the sections. In no case are they mentioned as being abundant, the usual designation being "very few."

The malignancy of any tumor is to be judged rather from a clinical than a histological standpoint. Thus we find that rodent ulcer when viewed from a microscopic aspect is a typical carcinoma, and that epulis is a typical sarcoma, yet each clinically has repeatedly been proved to be a fairly benign tumor. The question, then, which particularly interests the operating surgeon is what is the ultimate fate of the patients from whom primary cancers of the appendix have been removed?

Duration of Reported Cures. The after-histories of a number of the patients have been recorded, and the durations of the cures in the following instances are given:

Well after	9 years,	2 cases,	Jalaguier, McCosh.
" "	5½ "	1 case,	Driessen.
" "	5 "	3 cases,	Rolleston, H. Kelly (2 cases).
" "	4 "	3 "	Wiener, Lecene, Fauldner.
" "	3 "	4 "	Wier, Warthin, Cullingworth and Corner, Zaaijer.
" "	2 "	8 "	Moschkowitz, Eccles, Hurdon, Zaaijer, Mandlebaum, Grieg, Jong, Thorndike.
" "	1½ "	4 "	Moschkowitz, Zaaijer (2 cases), McBurney.
" "	1 year,	2 "	Battle, Burnham.
" "	7 months,	2 "	Zaaijer, Jones and Simmons.
" "	6 "	1 case,	Zaaijer.
		30 cases.	

Of the 90 cases in the two series, there were 79 cases operated upon. Of these, 13 were well three years or more after the operations, or 16 per cent., and 21 were well two years or more after the operations, or 26 per cent. Of course, many of the operations were of recent date, and the permanency of the cures is still sub judice.

PROGNOSIS. It is a remarkable fact that primary cancer of the appendix, which microscopically appears to be a malignant growth, is a relatively benign tumor when viewed clinically, since it does not tend to involve the lymphatics nor to form metastases. Recurrences after operation are almost unknown. This apparent benignity seems to be an exception to the rule that the younger the patient with a malignant growth, the more malignant is that growth. This must simply be accepted as a fact without adequate explanation. Cullingworth and Corner, and also Battle, suggest that perhaps the accompanying inflammation destroys the growth, by the sloughing of the offending organ, or the patient dies from peritonitis, or the growth is removed because of the coincident inflammation before dissemination occurs. It must further be remembered that when these growths have become extended, as undoubtedly occurs, they lose all their characteristics as appendical neoplasms, and they are then recognized as cecal cancers only.

In the 79 patients making up the series of Rolleston and my own, who were operated upon, there was only 1 (1.2 per cent.) in which the growth is definitely known to have recurred. This is the case of Lejars. A secondary operation, four months after the first one, showed a cancer of the cecum. The patient succumbed shortly afterward.

An interesting case is related by Lanz[4] of a probable recurrence after operation of a primary cancer of the appendix. It is not included in my series, because there was no microscopic examination of the appendix at the time of the operation. A man, aged forty years, suffered from symptoms of chronic appendicitis. At the operation, the appendix was found adherent and its tip was swollen like a "drumstick." A section of the appendix showed at this latter point a hard tissue mass, which was considered to be a "scar." A recurrence took place, and it was by this only that the true carcinomatous nature of the "scar" was recognized. A similar case is described by De Ruyter,[5] in which at autopsy a carcinoma was found to have developed in the stump of an appendix which had been removed six years previously. This case, for a like reason, is not included in my series.

Secondary growths, including cancerous lymphatics, were recognized as occurring in very few cases. In my own series of 48 cases there were only 2 in which mention is made of any such. These were the patients of Hartmann (XXXI) and Baldauf (IV), in each of which there was a small metastatic cancerous mass in the mesoappendix. In Rolleston's series of 42 cases there were 4 such cases, namely, Beger's patient, in whom the retroperitoneal glands were implicated, the 2 patients of A. O. J. Kelly and of Elting, in both of whom there were multiple growths on the peritoneum, and

[4] Beiträge zur klin. Chir., 1907, Band liv, p. 261.
[5] Archiv f. klin. Chir., Band lxix, p. 281.

Whipham's patient (autopsy), in which there were growths in the liver and right ovary. Thus, we find that in only 6 cases out of 90 in the combined statistics of Rolleston and myself, or 6 per cent., were there secondary growths. From the analysis of the cases in a preceding paragraph, in which there were enlarged glands at the time of the operations, it is seen that because glands are found enlarged, this is no reason for making a bad prognosis, since the microscope showed that only 1 case had cancerous lymphatics, the remainder being merely affected secondarily by simple inflammation from the appendices. Perhaps we may conclude, from the fact that fewer secondary growths were found in my series of cases than in Rolleston's, that appendices are removed more frequently now than formerly was the case for chronic symptoms, and at an earlier date and for slighter symptoms. By so doing, we undoubtedly will in future save a number of patients from developing cecal cancers, secondary to a primary growth in the appendix.

From the facts thus far deduced, it seems as though we should have to place these primary neoplasms of the appendix in a distinct class by themselves, so far as their malignancy is concerned, allying them somewhat in this regard with rodent ulcer and epulis, and in contradistinction to neoplasms of the alimentary tract generally.

Mortality of the Operations. All the patients in my series recovered after being operated upon, indicating that the presence of a primary appendical cancer does not prejudice the operative prognosis per se.

Surgical Significance of Appendical Cancers. These small neoplasms are not per se to be diagnosticated before operation. The symptoms are those of a simple appendicitis, usually of the chronic, recurrent type. Its age incidence corresponds to that of simple appendicitis. It probably occurs in about 0.4 per cent. of all cases of appendicitis, and this fact, if further confirmed in the future, will more surely cause us to advise appendectomy. The seemingly good prognosis of appendical cancers is more apparent than real, for histologically it has a malignant character with a tendency to involve progressively, though probably slowly, the meso-appendix and the cecum. Whether the cancer is the primary lesion and the appendicitis the secondary, or vice versa, makes absolutely no difference from the patient's standpoint. The main thing for him is to be rid of his cancerous appendix at the earliest possible moment.

Such an appendical cancer will almost always first be discovered by an operation. Benign tumors of the appendix are very rare, hence any circumscribed appendical tumor, found at operation, should always make one suspicious of cancer. In doubtful cases, a frozen section, made during the operation, would be of very great advantage, if possible to obtain; and in case of positive findings, a wide excision of the meso-appendix and removal of the lymphatic

glands should be practised. If the tumor be situated in the base of the appendix, it would be best to excise part of the cecum, otherwise this would not seem ordinarily to be a necessary procedure. As a frozen section at the time of the operation will rarely be available, it would be the part of wisdom to make a practice of removing habitually the entire meso-appendix in every operation for appendicitis, as this would not increase materially the risk to the patient under ordinary conditions. This practice is rendered advisable, first, because these tumors, even when very small, have a pronounced tendency to invade the meso-appendix; and second, because they frequently are invisible to the naked eye. Every removed appendix should be subjected to a careful microscopic examination.

When operating in the neighborhood of the appendix for reasons other than appendicitis, the appendix should be inspected carefully. If it has an irregular outline, or is clubbed at its extremity, or constricted, or presents a prominence on its surface, it should unhesitatingly be removed. I shall not go into the more debatable question of whether, in operations generally, the appendices should be routinely amputated in the absence of any visible abnormality. It seems, however, advisable to do so provided no extra risk would be incurred, since the appendix is such a potential factor for future harm for the patient in many directions. The practice of removing the appendix close to its junction with the meso-appendix should be deprecated.

RESUME. 1. Of the 76 patients operated upon for known reasons, 63 (83 per cent.) suffered from some variety of appendicitis. Of these, 23 (36 per cent.) were operated upon during or immediately after the first acute attack, while 40 patients (63 per cent.) had had symptoms of chronic appendicitis for varying periods of time. Of the entire 79 operated patients, 28 per cent. had had such chronic symptoms for a year or more. Eleven primary cancers of the appendix were found in appendices removed in the course of operations for other purposes, and were chance findings. In 2 other cases the operations were undertaken for the cure of iliac fistulæ. Ten primary cancers of the appendix were found in the course of autopsies.

2. In 78 cases in which the ages are recorded, it is found that there are 47 patients (60 per cent.) whose age was under thirty years. This age incidence corresponds very closely to that of ordinary inflammatory appendicitis, in which, in 3000 cases, 69 per cent. occurred before thirty years.

3. In 77 cases of primary cancer of the appendix in which the sex is recorded, we find that there were 44 females (57 per cent.) and 33 males (42 per cent.). In 3000 cases of simple, inflammatory appendicitis, 62 per cent. occurred in men and 38 per cent. in women. The reason for this almost complete reversal of frequency

in the two sexes in the two affections remains as yet entirely inexplainable.

4. Concretions apparently form no role in the etiology of primary cancers of the appendix, since in 90 cases they were found only 5 times (5.5 per cent.). This is in sharp contrast to the 984 times fecal concretions were recorded as occurring in 3403 operations for simple, inflammatory appendicitis, or 28 per cent.

5. In 71 cases in which the situation of the tumors was recorded, it is found that in 59 per cent. the neoplasms were located at or near the tip, and in 76 per cent. they were situated at or distal to the middle. This indicates that primary cancers of the appendix develop in the regions where strictures, obliterations of the tip, and chronic inflammatory lesions most commonly occur.

6. Enlarged lymphatic glands were recorded as being present in 8 cases, or 9 per cent. In 4 of these cases, microscopic examinations showed that there was no cancer in them, and in 1 case such secondary cancerous involvement was found. Hence we must infer that these primary cancers of the appendix are exceedingly slow in involving the lymphatics. Three cases are not recorded as having had the enlarged glands examined microscopically.

7. In 42 cases out of my 48 in which it is recorded, no tumors were visible to the naked eye in 14 cases, or 33 per cent. In 23 cases, or 55 per cent., one or more solid tumors were visible. Cysts were present in 3 cases, or 0.7 per cent. Perforations were present in 2 cases. Ulcerations were found in 2 cases. From these statistics it is evident how fallacious it is to argue that because there is no visible tumor, consequently there is no cancer present. Hence the inaccuracy of any statistics based solely on the macroscopic appearances of the appendices.

8. The frequency of occurrence of primary cancer of the appendix is approximately shown in the fact that 26 such cancers were found in 6505 appendices, or 0.4 per cent. This percentage is not absolute, because it is not stated in just what proportion of these cases microscopic examination of the appendices was made; presumably such examinations were made in but a small proportion. In addition, cecal cancers undoubtedly develop from primary appendical cancers, in which case the latter lose all their characteristics as the primary lesion, and are overlooked as such. From all of which we may conclude that a conservative estimate would place the occurrence of primary cancer of the appendix as not lower than 0.4 per cent. of all the appendices removed, or 1 in every 258 appendices examined. Positive proof of this estimate can only be established when a large series of microscopically examined appendices is brought forward.

9. In 71 cases it was possible to make a pathological classification of the neoplasms. Twenty-two per cent. were columnar-cell cancers, 53 per cent. were spheroidal-cell, 9 per cent. were of the

transitional type, and 4 per cent. were colloid cancers. The average age in the spheroidal-cell tumors was twenty-three years and in the columnar-cell type it was forty-three years, a difference in the age incidence in the two varieties of twenty years. Thus, we see that the spheroidal-cell cancers primary in the appendix are 30 per cent. more frequent than the columnar-cell variety. The frequency of occurrence of the two varieties in the appendix is very similar to that in neoplasms of the stomach, while in the intestines alone the columnar-cell type occurs in about 72 per cent. of the cases.

10. Of the 48 cases in my series, there are records regarding the microscopic extent of the growths in the appendices in 31 cases. In 15 cases, or 48 per cent., all the coats of the appendix were invaded, while in 7 cases, or 22 per cent., the meso-appendix in addition was involved in the growth. Thus these neoplasms show a tendency progressively to infiltrate contiguous structures, but without evincing evidences of producing distant metastases. This invading characteristic is probably of slow growth, as is further evidenced by the fact that in all the cases mitotic figures are designated as being very few.

11. Out of 90 patients with primary cancer of the appendix, there were secondary growths present in 6 (6.6 per cent.).

12. In 79 of the patients who were operated upon, the duration of the reported cures is given in 30 instances: 7 patients were well five years or more after the original operations, 13 were in good health three years or more afterward, while 21 showed no signs of any recurrence two years or more after the operations. In only 1 instance out of the 79, or 1.2 per cent., is it definitely stated that the growth recurred. From the facts deduced in this article, it would seem as though these primary tumors of the appendix should be placed in a distinct class by themselves, so far as their malignancy is concerned, allying them somewhat in this regard with rodent ulcer and epulis, and in contradistinction to malignant neoplasms of the alimentary tract generally.

13. The mortality in my series of 46 operations was nil, which indicates that the presence of a primary appendical cancer does not prejudice the operative prognosis per se.

14. The symptoms of these appendical cancers are not sufficiently characteristic to make a diagnosis per se possible without operation.

15. Any circumscribed tumor in an appendix should always arouse suspicions of cancer, following which the meso-appendix should be widely excised and enlarged glands removed. It will be necessary to excise part of the cecum only when the tumor is situated in the base of the appendix.

16. In every appendectomy the entire meso-appendix should be removed if possible.

17. Every removed appendix should be examined microscopically.

18. When operating in the neighborhood of the appendix for reasons other than appendicitis, the appendix should be amputated

in case it presents any abnormality, particularly when its tip is clubbed.

19. In addition to the cancers themselves found in the appendices, in 30 cases out of 48 in my series, or 62 per cent., it is found that chronic inflammatory lesions were discovered by the microscope. Whether the chronic changes are primary and the cancers secondary to these, or vice versa, it seems impossible to decide in the present state of our knowledge of the subject.

ADDENDUM.

Since this article was written, I have found the following additional 15 cases.

Letulle[6] has written a very beautifully illustrated article describing 11 cases which he personally has seen. Two of these are reported in the above article, namely, those of Jalaguier and Nélaton, while the remaining 9 are not so included. Of these 11 cases, only four cancerous appendices were removed at operation, while seven were discovered at autopsy. It is a remarkable observation that 4 of these latter cases were found in tuberculous patients.[7] Some of these cases illustrate unusual conditions.

Gayet[8] reports a case in which a cancerous appendix was found in a hernial sac, exactly similar to the condition narrated in Patel's case in the above article.

Vassmer[9] relates a case of primary cancer in a gangrenous appendix with peritonitis. The patient died after a secondary enterostomy.

Lubarsch[10] reports the case of a seventeen-year-old boy in the tip of whose appendix, at autopsy, a pea-sized cancer was found.

Weber[11] reports the case of a man, aged forty-three years, who was operated upon for the removal of a ventral hernia, following an operation three years previously for a large appendical abscess. A fist-sized tumor was found in the cecal region which proved to be an adenocancer of the appendix. Recovery.

Lothrop[12] reports operating upon a girl, aged nine years, for an acute gangrenous, perforative appendicitis, with abscess formation. On gross examination, nothing unusual was noticed in the appendix, but later microscopic examination revealed in its centre a primary cancer. The patient recovered. Her youth is noteworthy.

White[13] reports a case of colloid carcinoma of the appendix.

[6] Revue de gynec. et de chir. abdom., Tome xi, No. 5, Sept.–Oct., 1907.
[7] For a discussion of this association, see Letulle, Bull. Soc. Anat., July, 1903, p. 638.
[8] Revue de gynec. et de chirurgie abdom., 1907, vol. xi, No. 4, p. 687.
[9] Deut. Ztschr. für Chir., 1908, xci, 446.
[10] Verh. der Deutsch. Path. Gesell., 1907, p. 208.
[11] Petersb. med. Woch., 1906, No. 22, ref. Deut. med. Woch., 1907, p. 1110.
[12] Boston Med. and Surg. Jour., April 2, 1908, p. 450.
[13] AMER. JOUR. MED. SCI., 1908, CXXXV, 702.

PRIMARY CARCINOMA AND ENDOTHELIOMA OF THE VERMIFORM APPENDIX.

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In 1900, through the courtesy of Dr. John B. Deaver, surgeon-in-chief to the German Hospital, I was enabled to report 6 cases of tumor of the vermiform appendix—2 cases of fibromyoma, 2 of primary carcinoma, 1 of primary endothelioma, and 1 presumably of secondary carcinoma.[1] At the time of that report I was able to find in the literature the reports of only 18 additional cases of primary carcinoma of the appendix, and some of these were doubtful, that is, doubtful whether the disease was carcinomatous, and whether the newgrowth was primary in the appendix. Since then, however, considerable interest has been manifested in tumors of the appendix, stimulated in part at least by the accidental finding of many of the carcinomas in cases in which their existence was unsuspected until a microscopic examination of the excised organ had been made, and by the comparative youth of many of the subjects.

In 1905 I was able to collect from the literature 25 additional cases, making together a total of less than 40 undoubted cases of primary carcinoma of the appendix.[2] Since then several excellent studies of cases observed personally and collected from the literature have been published, of which it suffices perhaps to mention that by Rolleston and Jones,[3] who collected 42 undoubted cases, and that by McWilliams,[4] who has collected 105 cases.

My first report was based upon a macroscopic and microscopic study of 706 appendices removed at operation by Dr. Deaver during 1897, 1898, and 1899. Subsequently to 1900, although I continued to examine the excised appendices more or less cursorily, that is, with the unaided eye, a microscopic examiniation was made only in those cases in which it was specially requested, or in which the gross appearances suggested lesions of interest. On January 8, 1906 (appendix No. 3097), macroscopic and microscopic examinations of all excised appendices were resumed and have been continued to the present time. During this period 4 additional cases of primary tumor of the appendix have been encountered, which, again through the courtesy of Dr. Deaver, I am enabled to report herewith. The

[1] A Treatise on Appendicitis, by John B. Deaver, second edition (chapter on the Pathology, p. 95), and Univ. Med. Mag., May, 1900.

[2] A Treatise on Appendicitis, by John B. Deaver, third edition (chapter on the Pathology, p. 143).

[3] Primary Malignant Disease of the Vermiform Appendix, Amer. Jour. Med. Sci., 1906, cxxxi, 951.

[4] Primary Carcinoma of the Vermiform Appendix, ibid., 1908, cxxxv, 822.

total number of appendices examined up to May 1, 1908, is 4822, of which about 2500[5] have been examined microscopically. A rough estimate of the incidence of tumors in diseased appendices giving rise to symptoms may be based upon the number examined microscopically: including only the 5 cases of primary carcinoma, the incidence is 0.2 per cent.; including also the 2 cases of primary endothelioma, the incidence is 0.28 per cent.

An effort has been made to trace the subsequent history of the cases previously reported:[6] Case II, Endothelioma of the Appendix: A woman, aged twenty-four years at the time of operation (March 24, 1898), on February 28, 1908, had had no recurrence, and was perfectly well as far as abdominal conditions were concerned, with the exception of slight constipation. Case III, Carcinoma of the Appendix: A man, aged nineteen years at the time of operation (March 12, 1899), on February 5, 1908, had been in rather poor health since the operation, having sharp pains at times in the right iliac fossa, and the incision being tender at all times; he has had no further operative interference. Cases I and IV could not be traced.

The following is the report of the four additional cases (continuing the orginal numbering):

Case V.—S. B., a married woman, aged twenty-three years, was admitted to the German Hospital January 24, 1906. The family history and the previous medical history are irrelevant aside from the fact that in 1901 the patient had an attack of appendicitis, associated with severe pain in the right side and vomiting, that confined her to bed for three weeks. Four weeks prior to admission to the hospital she was suddenly seized with cramp-like pain in the right iliac fossa, associated with nausea and vomiting. She was confined to bed for one day, but tenderness at McBurney's point persisted for three days. On the day of admission to the hospital there was a recurrence of the pain, but otherwise the patient felt well. Constipation had persisted since the original attack. On admission the patient was found to be poorly nourished. There was tenderness in the region of the appendix. The leukocytes were 10,200 to the cubic millimeter. The temperature ranged from 99.4° to 97.4°, and the pulse from 108 to 72. The urine contained no albumin, no sugar, and no casts.

On January 27 Dr. Deaver removed the appendix, finding it kinked on itself and curled about the cecum. The patient made an uneventful recovery, and was discharged cured on February 7, 1906. On February 11, 1908, information was obtained that the patient was in good health, that she had had no symptoms since the operation, in particular that there had been no intestinal disturbances.

The following are the notes of the examination of the appendix

[5] This number is approximate only, but it is probably an underestimate.

[6] This was kindly undertaken by Dr. A. D. Whiting, assistant surgeon and registrar to the German Hospital.

(No. 3124): The appendix is curled and twisted upon itself, and makes up a mass of tissue 4.6 x 2.5 cm. On section the organ is seen to be obviously the seat of a newgrowth, grayish white in color and somewhat granular, invading all the coats and causing considerable increase in the thickness of the wall. Longitudinally it extends from the tip almost if not quite to the proximal end. The lumen is quite devious in course and almost completely occluded except toward the proximal end, where there is a small area of dilatation filled with softened necrotic material. The mucosa throughout is roughened, apparently considerably ulcerated and necrotic. Microscopically the appendix exhibits the lesions of chronic interstitial appendicitis, with some acute exacerbation; that is, there is considerable increase in the fibrous tissue in the submucosa and the muscularis, much hyaline metamorphosis, atrophy of the muscularis, and more or less perivascular round-cell infiltration. In addition, the mucosa is wanting throughout, the free internal surface consisting of an exuberant proliferation of epithelial cells arranged in nests of varying size and shape, supported by a well-developed connective-tissue stroma, doubtless the remains of the submucosa. For the most part these epithelial cells are the seat of mucoid degeneration; many of them have completely lost their individual identity and appear as more or less necrotic debris. There is a varying degree of epithelial infiltration of the muscularis, extending in some places almost if not quite to the serous coat, in which regions the identity of the individual epithelial cells is much more apparent than in the submucosa.

Diagnosis. Mucoid (colloid) carcinoma of the appendix; chronic interstitial appendicitis with acute exacerbation.

Case VI.—F. L. B., a single girl, aged seventeen years, was admitted to the German Hospital February 27, 1906. One brother died of carcinoma of the stomach; otherwise the family history and the previous medical history are irrelevant. Eight hours prior to admission to the hospital the patient was seized with acute abdominal pain, at first general in distribution, but gradually becoming localized to the right iliac fossa. On admission she was a well-developed, well-nourished girl. The abdomen was markedly rigid on the right side and very tender over McBurney's point. No mass was palpable. The urine contained no albumin, no sugar, and no casts. The temperature was 99.6°, and the pulse 100.

On February 27 Dr. Deaver removed the appendix, which was found non-adherent; there was no free fluid in the peritoneal cavity. The patient made an uneventful recovery, and was discharged cured on March 12, 1906.

The following are the notes of the examination of the appendix (No. 3181): The specimen consists of an appendix 9.5 cm. long, and from 0.9 to 1.2 cm. in thickness, the distal 6 cm. being the more distended. The serosa is covered with a fibrinoplastic exudate and reveals marked injection of the vessels. On section the distal dilated

portion is found to be separated from the proximal portion by a well-marked constriction, and to be filled with sanguinopurulent material; the wall is very thin, the mucosa much ulcerated and reveals many small submucous hemorrhages. (A newgrowth was not observed until the microscopic examination was undertaken, when it was seen macroscopically as a small infiltration of the submucosa, 2 to 3 mm. in diameter, opposite the attachment of the mesentery, and extending 1.5 cm. from the constriction near the middle of the appendix toward the proximal end.) Microscopically there were the lesions of acute appendicitis of moderate grade: vascular dilatation, œdema, round-cell infiltration, and foci of hemorrhage in the mucosa and submucosa, and loss of considerable of the epithelial covering of the mucosa. The newgrowth consists of narrow columns of cells, usually not more than two cells in width, but ten or more cells in length, infiltrating the spaces of the connective tissue of the submucosa. The collections of cells often taper to a point at their extremities, although in some regions they are ovoid or rounded, and have apparently quite an intimate relationship with the surrounding connective tissue; in some regions a plexiform arrangement, or anastomosing network, of the columns of cells may be made out; in other regions the origin of the cells from the endothelial lining of the lymph channels is obvious in their lining such spaces, which here and there are somewhat dilated, and in their gradual increase in size and thickness. The individual cells vary somewhat in shape, but, as a rule, they are ovoid or elongated, corresponding with the shape and direction of the lymph spaces that they line; toward the extremities of many of the spaces the cells are quite flattened. The nuclei for the most part are ovoid or elongated, stain well, and are rich in chromatin. The supporting connective tissue contains relatively few cells; it is largely homogeneous and evidently the seat of hyaline degeneration.

Diagnosis. Endothelioma of the appendix; acute appendicitis.

CASE VII.—L. B., a single woman, aged twenty-seven years, was admitted to the German Hospital December 30, 1907. The family history and the previous medical history are irrelevant aside from the fact that the patient had typhoid fever at the age of nine years. Two years prior to admission to the hospital she had a severe attack of pain in the right upper abdominal quadrant, with radiation to the right shoulder, a chill, but no vomiting. Subsequently she was jaundiced for two months. The pain has been almost continuous since, and there have been several acute exacerbations. The patient has been markedly constipated, but there have been no other digestive disturbances; nor have there been continued chills, fever, or sweating. On admission the patient was well developed and well nourished. There was some tenderness along the right costal margin and slight rigidity of the upper part of the right rectus muscle. The temperature was 99°, the pulse 52 to 92. The urine contained no

albumin, no sugar, and no casts. The hemoglobin was 78 per cent., the leukocytes 6500, and the coagulation time ten minutes. Examination of the stools revealed no parasites and no eggs; the occult blood test was faintly positive.

On January 4, 1908, Dr. Deaver operated, making an incision through the upper part of the right rectus muscle. The gall-bladder was found normal and to contain a small amount of bile, which was readily discharged through the biliary ducts. The surrounding organs also appeared to be normal. The wound was closed, and a second incision was made over the region of the appendix and the appendix was removed. The patient made an uneventful recovery, and was discharged cured January 18, 1908.

Th following are the notes of the examination of the appendix (No. 4594): The appendix is 8 cm. long, and 0.3 cm. thick, except at its distal extremity, where there is a bulbous enlargement 1.3 cm. in thickness and 3 cm. in the length of the organ. The vessels of the serosa are somewhat injected. The lumen is almost completely occluded by swelling of the mucosa, except in the region of the bulbous enlargement, where, although there is increase in thickness of the mucosa and the submucosa, there is also an obvious lumen containing a small amount of turbid fluid. (A newgrowth was not observed on macroscopic examination, but was subsequently found to comprise a small nodule, about 3 mm. in diameter, opposite the attachment of the mesentery, and extending 2 cm. from the tip of the organ.) Microscopically the lesions of chronic interstitial appendicitis with acute exacerbation are apparent; that is, there is considerable connective-tissue hyperplasia with hyaline metamorphosis, vascular dilatation, œdema, round-cell infiltration, foci of hemorrhage, and shedding of the epithelial covering. The newgrowth in the distal end consists of nests of cells of varying size and conformation, supported by a well-developed connective-tissue stroma; the submucosa especially is the seat of the epithelial infiltration, but there is also a moderate infiltration of the muscularis, even to the subserosa, where the nests of cells are usually large. The individual cells are epithelial in type, of moderate size, polyhedral in shape, and have clear vesicular nuclei that stain well.

Diagnosis. Carcinoma of the appendix; chronic interstitial appendicitis with acute exacerbation.

Case VIII.—M. K., a single woman, aged twenty-eight years, was admitted to the German Hospital January, 1908. The family history and the previous medical history are irrelevant. The present illness began three days before admission to the hospital with severe cramp-like pain in the abdomen, that soon became localized in the right iliac fossa, nausea and vomiting, but no chill. On admission the patient was well developed and well nourished. There was marked tenderness and rigidity on the right side rather high up (about the level of the umbilicus), and a mass was palpable. The

hemoglobin was 88 per cent., and the leukocytes 25,800. The temperature varied up to 103°, and the pulse up to 132. The urine has a specific gravity of 1015 to 1031, revealed a faint trace of albumin, but no sugar and no casts.

On January 11 Dr. Deaver operated. On opening the peritoneum considerable pus was evacuated. The appendix was found acutely inflamed, perforated, and adherent to the colon; it was removed. The patient made an uneventful recovery, and was discharged on the thirtieth day after operation with a granulating wound.

The following are the notes of the examination of the appendix (No. 4609): The appendix is 6 cm. long and from 0.6 to 1.5 cm. in thickness. There is marked injection of the vessels of the serosa. The tip is much dilated—the lumen to 0.8 mm. in diameter, and contains a hard calculus; here the wall is reduced to 3 to 4 mm., the mucosa is rough, ulcerated, and reveals small foci of hemorrhage. Elsewhere the lumen is variously dilated and constricted, the mucosa roughened, and shows foci of hemorrhage. (The newgrowth was not detected macroscopically, and even after it had been found microscopically there was nothing to suggest its presence to the unaided eye.) Microscopically the appendix reveals slightly increased fibrosis of the submucosa and muscularis, and the ordinary phenomena of acute inflammation: vascular dilatation, œdema, cellular infiltration, foci of hemorrhage, shedding of the epithelium, etc. The newgrowth is limited to the dilated peripheral extremity of the organ, and is almost if not quite annular. It consists of nests of cells supported by a well-developed connective-tissue stroma, obviously, in part, at least, remains of the submucosa; the mucosa is almost if not quite missing. There is a moderate infiltration also of the muscularis, especially near the subserosa. As a rule, the nests of cells are very large. The individual cells are epithelial in type, of moderate size, polyhedral in shape, and have clear vesicular nuclei that stain well.

Diagnosis. Carcinoma of the appendix; acute ulcerative appendicitis with perforation.

THE SURGICAL ASPECTS OF DUPUYTREN'S CONTRACTION.

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With the expansion and better grouping of surgical knowledge, there is a strong tendency to do away with the names of those surgeons who have first described conditions or who have been indubitably associated with them. However wise such a procedure may

be from the scientific standpoint, one who is interested in the history of surgery cannot but regret the change. But there are some conditions to which the names of their investigators are tightly forged, and I have no doubt that in the years to come the name of the great French surgeon, whose strong convictions and firm insistence first compelled a hearing, will be associated with contraction of the palmar fascia. Basing his beliefs on the dissection of a case, he proclaimed his findings in 1831,[1] and with that self reliance and personal assurance which was so characteristic of him, showed the falsity of the then current opinion that the deformity was due to the contraction of the tendons. In his "Leçons Orales," in 1832, and his lectures, delivered in 1833, he reiterated time after time his beliefs, winning acceptance by the force of his persuasion. Henry Cline, in his lectures of 1808, and Sir Astley Cooper, a little later, allude to the true character of the deformity, but their opinions were not backed by pathological observations.

An extensive literature has grown up around Dupuytren's first dissection, which has served to confirm and expand his principles. Although the contraction is fairly common, the subject is treated so briefly, and many times incorrectly, in our surgical treatises, that I have thought it advisable to review the main facts in the anatomy, pathology, and etiology of the disease before proceeding to discuss its radical treatment.

The onset of Dupuytren's contraction is most interesting. A middle-aged or elderly man will notice that his ring- or little finger is somewhat stiff, and will often assign the cause to rheumatism, with which he may have been previously afflicted. Local pain may be slight or entirely wanting, but he finds that extension of the affected part is in some way impeded. As the months pass and the condition does not improve he may notice that there is a slight puckering of the skin over the metacarpophalangeal joint, as if a subcuticular suture had been gradually tightened. Later, small and hard nodules appear, and the hills and valleys, which have been noticeable in the palm, become more marked. The disease proceeds insidiously; the joints gradually increase their flexion, and there are seen in the palm, along the lines of the flexor tendons to the affected fingers, hard, unyielding bands, to which the skin seems to be most intimately attached. A long period of time has elapsed since the first symptoms, and the trouble may now be spreading to adjacent fingers, which, in turn, begin to contract; the palmar bands become more noticeable, and the furrows between them deepen. Flexion may be so pronounced that the finger-nails press into the flesh of the palm, and the patient's condition is pitiable. Forcible extension is impossible, and the contracted, deformed hand is of little or no service.

[1] Journal universal et hebdomadaire de médecine et de chirurgie pratiques, Paris, 1831.

To Adams,[2] who first brought the pathology and surgical treatment into general notice in England, and to Keen,[3] who performed a similar service in this country, we owe much. From the statistics of Keen (23-personal cases and 95 cases from the literature), Noble Smith[4] (70 cases), and Nichols[5] (50 cases), we may deduce the following facts: The disease occurs in men of all classes and generally after the fortieth year. It is met with but seldom in women, and Adams states that he considers it about ten times as common among men. The two hands are attacked in nearly equal proportion, the disease showing a decided preference for the ulnar side, originating in the ring or little finger or in both. Its hereditary character is worthy of mention. Adams has noted it in several cases, and Keen found it in nearly one-third of the records. Adams has stated that the disease is largely due to gout, and Keen has emphasized the fact that it is found connected with a gouty or rheumatic history. Smith states that his inquiries were against these conditions being the cause, while Nichols fails to find that the disease is a manifestation of, or results from, rheumatism. In many cases the hands are affected symmetrically. Of its frequency we have various testimony, but the largest statistics have been compiled by William Anderson.[6] He states that of 2600 adults of the poorer classes in English infirmaries, about five-sixths of whom were over middle age, 33 (1.27 per cent.) were affected.

If we make a careful dissection of the fingers and palm, we find that directly under the skin and above the fascia proper is a dense layer of fibro-areolar tissue, the superficial palmar fascia, perhaps more marked on the ulnar side of the palm than elsewhere, and extending well up on the fingers. The fibers are thin, but very strong, and they form a sort of web, which is everywhere filled by fatty tissue. Traversing this layer are a very great number of strong fibers which closely bind the skin to the fascia below, and are best appreciated by the dissector by the gritty feel which they impart to the scalpel. These are particularly noticeable upon the ulnar side. This cross fibrous layer is not emphasized in our anatomies, but its bearing on Dupuytren's contraction is most important. It will be remembered that the contraction first involves the ulnar surface of the hand.

Below this there is the deep palmar fascia, satisfactory descriptions of which are given in our anatomical text-books. Arising

[2] Observations on Contractions of the Fingers, London, 1892. Remarks on the Contraction of the Fingers, Proc. Med. Soc. London, 1879–81, v, p. 132. Dupuytren's Contraction of the Fingers in Women, Brit. Med. Jour., 1882, i, 84.

[3] Etiology and Pathology of Dupuytren's Contraction of Palmar Fascia, Proc. Phila. Co. Med. Soc., 1881–82, iv, 108; also Phila. Med. Times, 1881–82, xii, 370.

[4] Brit. Med. Jour., March 29, 1884, p. 603.

[5] A Clinical Study of Dupuytren's Contraction of the Palmar and Digital Fascia, AMER. JOUR. MED. SCI., 1899, cxvii, 285. Histology of Dupuytren's Contraction of Palmar Fascia, Med. News, 1889, lxxv, 491.

[6] Deformities of the Fingers and Toes, London, 1897.

above from the annular ligament and the palmaris longus muscle, it spreads fanlike over the palm, its firm, fibrous bundles being inserted into the lateral margins of the anterior ligaments of the metacarpophalangeal joints of the four fingers. Some fibers, however, go to the bases of the first phalanges, while others go to their sides and reach down even to the second and third phalanges. Besides these, there are median fibers extending down each finger to the base of the second phalanx.

To the surgeon who performs an open operation for the relief of this contracture, certain of these bands lying in the axes of the fingers appear as large, firm, and very resistant cords stretched tightly across the palm, as is stretched the string to a bow. Above these fibers the subcuticular tissue is very thin or entirely lacking, and so thick are these cords at times that they often have been mistaken for the flexor tendons. This is an error which the best of surgeons have made, and is commented upon by all those who have written extensively of the operative interference. There is no doubt that, in some operations, after the skin has been carefully dissected away from the bands and the fingers fairly well freed, by incisions along their surfaces, the large bands of the offending fascia have been left in situ. If the operator will but go a little deeper, he will find the flexor tendons lying in their sheaths. Again, the fibrous bands will at once be recognized from the fact that they are inserted on the base and sides of the first phalanx. This is not the case with the tendon; it does not divide here, neither does it have an attachment to the first phalanx. Again, the finger tips may be inserted beneath the bands, whereupon the movements of the flexor tendons are readily appreciated.

Microscopic examinations have been made by a number of observers, notably Richer,[7] Chevrot,[8] Langhans,[9] Anderson,[10] and Nichols,[11] and the following facts observed: The stratum corneum has been found by some to be thickened, while others have denied skin changes. It is probable that they do not take place, if at all, until late in the disease. The contracted bands are found to consist of very dense and firm fasciculi longitudinally arranged. They are, in general, similar to the normal fascia, which may lie adjacent to them, the bands being but a hypertrophy of a circumscribed tract. In cases in which the contraction is fairly recent, these fasciculi are well mixed with connective tissue elements and bloodvessels, but in cases in which the contraction has extended over a period of years these fasciculi are fused into a homogeneous mass and the cellular and vascular elements, which were earlier present, have entirely disappeared.

[7] Progress médicale, Paris, 1877, v, 369.
[8] Recherches sur la rétraction à l'aponeurose palmaire, Paris, 1882, p. 21.
[9] Quoted in Brit. Med. Jour., January 10, 1891, p. 62.
[10] Loc. cit.
[11] Loc. cit.

While this picture points to a definite hypertrophy, its causation is obscure and has led to much speculation. Dupuytren held the opinion that the disease resulted from slight local traumas, and there are certain facts to be mentioned in favor of this view, and others against it. Adams and Keen gave gout a prominent place in the etiology, while many have thought that rheumatism lay at the bottom of the trouble. Still others have placed the disease among the nervous disorders, and their claims will be set forth later.

In the instances of the contraction which have come under my notice I have seldom failed to elicit some history of trauma. In some cases the trauma has been severe; in others, but slight. Habitual contracture, as in handling a shovel or driving a team, has been now and then complained of. The traumas were of the most varied kinds, and, feeling that there is a strong tendency on the part of patients to find an outward and material cause to account for such deformities, I have not laid much stress on these portions of their histories.

Recently, however, I have operated on a case of contracted fascia in which the history of trauma was most perfect and in which the evidences of trauma are still present. The patient, an intelligent man of forty-two, is firmly convinced as to the origin of his trouble. He has worried much over it, and has carefully watched the progress of the disease. The account which he gives of its onset and its gradual development is most complete. He states that it dates from four years ago, when he received an abrasion over the metacarpophalangeal joint of the little finger, left hand, while lifting some heavy timber in a mine, work to which he was unaccustomed. A calloused surface formed, which soon peeled off; the part has never healed properly, and has since remained a constant source of irritation. About two months after the beginning of his trouble he noticed that he could not fully extend his finger, and that there were a few hard nodes contiguous to the abrasion, lying in the palm in the axis of the little finger. These coalesced into a cord, and at the time of operation this fibrous band was sharply marked upon the surface, the skin over it being elevated and firmly adherent to it. The finger was contracted almost to a right angle, and the last phalanx was flexed to its full extent, resting closely upon the second. The patient was of the opinion that some grit or fine gravel had been ground into the hand, and cautioned me carefully at the time of operation to look for such foreign material at the site of the abrasion. He bears no evidence of the existence of the disease in the other hand. His general health is very good, and he has never suffered from gout or rheumatism. The accompanying photograph was taken three weeks after operation. The scar in the palm is hardly noticeable, but the abrasion remains the same as before.

Another patient, on whom I operated some two years ago, was a dishwasher by occupation, and he came to me for amputation of his

ring finger, it being tightly flexed in the palm of his hand, due to contraction of the palmar fascia. The disease was of some four years' standing. Paronychia and excoriations and abrasions on the palms and fingers are common in this class of subjects, and the patient bore the marks of his occupation. He stated that his hands were habitually sore and tender.

Such a history as this is suggestive, but does not make an impression like the first case. Out of 50 cases examined, Nichols[12] found 15 which could be associated with more or less recent irritation or trauma. It is generally held by the older writers on the subject that gout and rheumatism are important factors in the etiology. Subsequent investigations have failed to verify this opinion, and personally I have not been able to trace any of my cases to such a causation.

Dupuytren's contracture apparently of traumatic origin. Photograph taken three weeks after the operation. Note the calloused surface at the metacarpophalangeal joint.

Of the nervous origin of Dupuytren's contraction much can be said, and it is at present the popular theory. Certainly the tingling and prickling sensations which are sometimes present in beginning cases are suggestive of the paresthesias of nerve lesions. Again, the fact that undoubted cases of heredity have existed is a difficult one to combat from the standpoint of simple trauma. We have no explanation to offer of the truth that it occurs on the ulnar side of the hand unless, as has been claimed, it arises from the fact that the skin is not as thick here, thus exposing the fascia to insult. Such an explanation seems hardly warranted. The condition of the fascia on this side has been commented on in considering the anatomy, but while it has a most important bearing on the clinical picture, we are not justified in going so far as to connect it with the etiology. That the disease is so often bilateral is certainly a strong point in favor of its nervous origin. Recently there has been a re-

[12] Loc. cit.

action against the nervous theory, and Ledderhose[13] believes that the beginning of the disease is an inflammatory proliferative process in the aponeurosis, and that subsequent trauma leads to the formation of nodules and finally to retraction.

The age of onset, which is generally past middle life, has been given as an argument for the nervous origin of the disease, and those who believe in a traumatic origin can only cite in rebuttal the disappearance of subcuticular fat with advancing years. If we grant that the condition is due to trauma alone we shall be obliged to admit that it should be met with much more frequently. As in other conditions, we cannot overlook an hereditary tendency or a predisposition on the part of the tissues. Taking this into account, Myrtle[14] has argued that, as in manual labor the skin becomes much thickened, this cause, an irritative hyperplasia, is competent to affect the underlying fascia.

It is probable that no single factor can satisfactorily cover the etiology, and it is interesting here to note Abbé's[15] theory of the origin of the disease: a slight traumatism, then a spinal impression produced by this peripheral irritation, following which comes a reflex disturbance at the seat of trauma, an insensible hyperemia, and pathological changes in the fascia.

From the consideration of the various degrees of the contraction, it is at once evident that no one method of operative interference will apply to all cases, and that the surgeon must adapt his procedure to the particular problem which confronts him. As one looks over the literature, he is struck by the excellent results and the wide range of application of the method of subcutaneous incision. This procedure, which was introduced in England by Adams and popularized in this country by Keen and Abbé, consists in dividing the contracting bands by many subcutaneous sections, a knife with a very narrow blade (Mr. Adams employing a blade of $\frac{1}{16}$ inch width) being used. It was necessary in severe cases to make many such incisions, Adams in one instance having used eighteen, and Abbé twenty-five. Such a method is difficult; it requires an accurate knowledge of the pathology of the disease and the anatomical topography, and, moreover, it does not appeal to our present ideas of surgical thoroughness. Yet the excellent results reported by the method in the hands of a number of observers, many of the cases having been followed over a period of years, show the curative value of operation and what great success may follow an incomplete procedure.

The operations which have been performed by those who have favored the open method have been characterized by long incisions or the making of extensive flaps in order to facilitate the complete

[13] Quoted in von Bergmann's Surgery.

[14] Dupuytren's Contraction of the Fingers, Brit. Med. Jour., 1881, ii, 894.

[15] On Dupuytren's Finger Contraction, its Nervous Origin, N. Y. Med. Jour., 1884, xxxix, 436; Further Remarks on Theory of its Nervous Origin, Med. Rec., 1888, xxxiii, 236.

removal of the offending fascia. Some have advocated the total excision of the skin of the palm, allowing the wound to granulate, or have sought to fill this extensive denudation by skin grafts or by a large flap taken from the back of the hand. Others have adopted a V-shaped incision, the angle of the V pointing toward the forearm, and, as such a flap is almost certain to slough, it has generally been excised at the time of operation. Parallel incisions have also been made, one on each side of the offending band, and the fibrous structure and the skin overlying it excised. Reviewing these radical operations, it is evident that here, as in so many other instances, the surgical pendulum has swung to its extreme in the opposite direction. We should not forget the good results reported by many observers with the subcutaneous operation and the fact that Adams, who probably had the largest experience in this field, has made the statement that the method is applicable in the severest cases. In extreme conditions a sacrifice of skin may become necessary, but such cases are not frequent. When the cords are very pronounced it will be found that the subcuticular fat has entirely disappeared, and the fibrous fascia is strongly adherent to the skin. Yet the skin can be saved by careful dissection.

I have begun my operation upon the contracted fingers instead of the palm. The parts being thoroughly cleansed, small incisions, running in the axes of the fingers, are made with a straight, sharp-pointed bistoury on the palmar surface and directly over the affected joints. An incision of 1 cm. or less is all that is necessary, except in very severe contractions. The skin and what subcuticular fat is present is then carefully dissected back on both sides, when the long fibrous bands will be seen. These are excised, and an endeavor then made to straighten the affected finger. This will usually not be possible, and it will be found necessary to pass the knife down deeply around the joint, the other hand serving as a guide outside, so as not to buttonhole the skin. A gritty feel warns the operator when he has arrived at the lateral fibers, which sometimes run nearly as far back as the extensor tendons. These are in turn divided. If the joint be a terminal one, and the bone has not become hypertrophied, it can now be brought to full extension. The same statement generally applies to the first phalangeal joint, but at the metacarpophalangeal articulation it will be necessary to cut the lateral insertions of the deep palmar fascia. These lateral insertions will have become changed into heavy cords, which are strongly adherent about the joint, while other thick fibers run to the sides of the phalanx. Besides these structures there will generally be a median cord, which must be excised. This, if present, will be firmly adherent to the skin over the joint and the shaft of the phalanx.

The fingers are now quite free, and it remains for the operator to remove the heavy fibrous bands which run in their respective axes. This can be accomplished through comparatively short incisions,

which I prefer to make slightly to the side of the summit of each band. The skin is then undermined on all sides, and it is surprising how much can be done through a small opening if the surgeon be possessed with the necessary patience and if he exert a proper amount of care. The band being freed, it is excised. In beginning cases portions of glistening palmar fascia, macroscopically as yet unchanged, are seen in the vicinity of the bands; these should be removed as thoroughly as possible. The palm should now be placed upon the stretch and carefully examined for other points of contraction. Bleeding is generally considerable; I prefer to control it, with this method of small incisions, by an Esmarch bandage about the wrist, being careful that hemorrhage has absolutely ceased before suturing. The edges of the wound are coapted by a through-and-through continuous suture of fine silk.

The fingers are placed in extension upon a dorsal wooden splint. Passive movements should be begun as early as possible; I have removed the splint and made these movements as early as the sixth day. The splint is omitted after the tenth day. The endeavor should be to perform the work thoroughly through a small incision, for operative wounds of the hands often do not heal kindly, and a large resulting cicatrix will not only be unsightly but may limit motion. I have done the operation under local cocaine anesthesia, but with the above technique I prefer a general anesthetic. Anesthesia for a period of a half-hour may be obtained by infiltrating the median and ulnar nerves with a 2 per cent. cocaine solution.

The method which I have here described is, in general, one which has often been employed, but I have outlined it in order to emphasize the fact that it is possible to perform the operation through smaller incisions than have heretofore generally been used.

TORSION OF APPENDICES EPIPLOICÆ AND ITS CONSEQUENCES.

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Although the anatomical nature of appendices epiploicæ has been thoroughly discussed, and loose bodies, or corpora aliena, in the abdominal cavity or in hernial sacs, resulting from torsion of their pedicles, have been reported at autopsy in quite a number of instances, until quite recently very little was known of their pathology. One of the earliest references to the pathological importance of appendices epiploicæ and their corpora aliena is contained in the

lectures on pathological anatomy by Wilks and Moxon[1] (1889), in which it is stated that "a surgeon found such a body in a hernial sac, and an altered appendix, still attached, was found to have caused the strangulation that made operation necessary." In 1894 Riedel,[2] of Jena, reported the removal of two corpora aliena which had given rise to symptoms of gallstone colic. No further communications appeared, however, until November 28, 1905, when Riedel[3] contributed a paper on "Torsion of Appendic s Epiploicæ and Its Consequences," with a report of 8 cases, of wnich the following is a *resume:*

CASE I.—Attacks of pain simulating gallstone colic; no tumor. Diagnosis of adhesion of gall-bladder. Two corpora aliena, almost as large as a cherry, were removed at the operation. Three years later the attacks recurred, and the patient committed suicide. At autopsy two more foreign bodies were found.

CASE II.—Student, aged twenty-five years. Four years ago an appendical abscess was opened, the distal end of the appendix coming away. Three indefinite attacks recently, apparently of appendicitis. At operation a yellow roundish foreign body 1.5 cm. long and 0.75 cm. thick slipped out of the peritoneal incision. The appendix, well closed distally, and apparently not inflamed, was lightly adherent to the cecum. Recovery.

CASE III.—Max B., aged thirty-two years; apparently typical attacks of gallstone colic, with jaundice. No tumor; vague tenderness in the region of the gall-bladder. At operation the liver showed numerous yellow plaques. The gall-bladder contained no stones; the bile duct was not distended. The omentum was adherent to the liver and the transverse colon, and two corpora aliena adiposa were lightly adherent to it. They were flat, roundish, calcareous bodies, one 0.75, the other 1.25 cm. long. A third body, still smaller, was lying free in the mesocolon. A number of appendices epiploicæ were hanging by a mere thread from the transverse colon, their distal ends not more than 2 or 3 cm. thick; none was twisted. Recovery.

CASE IV.—Mrs. W., aged forty-one years, symptoms of peritonitis, including fecal vomiting. Operation: Cloudy serum and shreds of fibrin in the peritoneal cavity. Jejunum and large intestine much distended; ileum less so. No appendicitis or cholecystitis. A crescentiform appendix epiploica, attached to the descending colon, with a flat, gray, foreign body about 1.5 cm. long and 1 cm. wide, lying free between it and the abdominal wall, was seemingly the sole cause of the peritonitis. The appendix epiploica was not twisted. Apparently it had straightened out after separation

[1] Lectures on Pathological Anatomy, 1889.

[2] Ueber Adasiv-Entzundungen in der Bauchohle, Arch. f. klin. Chir., Berl., 1894, xlvii, 153–215.

[3] Münch. med. Woch., November 28, 1905.

of the distal end. The peritoneal cavity was flushed out and the wound closed. Patient died on the third day. At autopsy no further cause of peritonitis was discovered. A luxuriantly growing bacillus, apparently Bacillus coli communis, was cultivated from the central part of the corpus alienum.

Case V.—Vomiting for fourteen days, finally fecal; general condition good. Operation: An oblong corpus alienum, somewhat constricted in the middle, and about as large as a bean, lay free in the peritoneal cavity. The parent appendix epiploica seemed to spring from the cecum, and was adherent to a coil of small intestine in such a way as to act as a constricting band. The small intestine was greatly distended. The appendix epiploica was easily removed. Recovery good.

Case VI.—Gustav Gerhard, aged forty years; obstruction of the bowels. Operation: Fluid in the peritoneal cavity; jejunum greatly distended; ileum less so. In the right iliac fossa, arising from the left wall of the cecum, an appendix epiploica stretched across the ileum and was adherent by its twisted middle portion to the mesentery of a coil of small intestine, and compressed the ileum firmly against the posterior abdominal wall; the distal end, about the size of a bean, and still attached to the twisted part, was gangrenous. The ileum was greatly contracted at the point of crossing. The appendix epiploica was quickly removed; the ileum was opened about 20 cm. above the obstruction and the entire small intestine, which was very much inflamed, was emptied of its contents. The patient died on the following day. Autopsy showed peritonitis of a mild grade, as had been demonstrated at the operation.

Case VII.—Hulda G., aged fifty-six years; admitted April 27, 1904. Eight days previously patient had complained of pain in left abdomen, and consulted a physician. In the right inguinal canal was a reducible hernia as large as a small apple, and on the left side, below Poupart's ligament, was a hard, insensitive, irreducible tumor of the size of a walnut, which, on operation, proved to be a femoral hernia. A necrobiotic appendix epiploica twisted once on its axis and adherent at the distal end was found in this hernial sac. Removal. Recovery.

Case VIII.—Anna B., aged twenty years; admitted August 14, 1905. Has had reducible femoral hernia on left side for two years and an irreducible femoral hernia on the right side for fifteen months. Was taken with abdominal pain on the afternoon of August 13; left hernia sensitive and irreducible, but was reduced spontaneously during the following night, after a hypodermic injection of morphine. At 2 P.M. of the next day a corpus alienum 1 cm. by 0.5 cm., hanging by a fresh and still bloody thread of fibrin, was found in the left hernial sac.

Virchow, who, as quoted by Riedel, has given us a careful description of corpora aliena in all their phases, mentioned a case in which

the patient died with symptoms of peritonitis, and at autopsy a hard body, larger than a cherry, was found free in the peritoneal cavity; the vermiform appendix was normal.

The fact that changes in the fatty appendices of the colon may give rise to pathological complications of such magnitude as those described by Riedel excited considerable interest among other observers. Six further cases have been reported during the brief space of time which has elapsed since the publication of Riedel's paper, and the literature now contains detailed accounts of 14 cases in which appendices epiploicæ, or resulting corpora aliena, necessitated surgical intervention. In 8 of these cases the appendices were situated in the hernial sac, intra-abdominally in the other 6.

Lorenz[4] reports a case of irreducible right labial hernia in a woman, aged thirty-three years, in which operation revealed a narrow, tense pseudoligament about 6 cm. long, among loops of intestine, inserted mesially to the neck of the hernial sac, and around which an appendix epiploica, arising from the colon, had become twisted and strangulated. The immediate parietal and visceral peritoneum was covered with fresh deposits of fibrin, and the twisted appendix showed several slight subserous hemorrhages and necrosis of the pedicle at the point of strangulation. The band and strangulated appendix epiploica were removed, the intestines returned to the abdomen, and the patient made an uneventful recovery.

Shortly after the appearance of Lorenz's article, v. Bruns[5] reported a case of irreducible left inguinal hernia in a woman, aged fifty-five years, who was suddenly taken with pain about eight davs prior to operation. The skin over the hernial area was red and œdematous. Incision allowed a small quantity of fluid to escape, and revealed a gangrenous strangulated appendix epiploica, which was removed. The patient made a good recovery.

Muscatello[6] reports 2 cases of hernial incarceration of appendices epiploicæ. One occurred in a woman, aged fifty-six years, who was suddenly attacked by violent femoro-inguinal pain, radiating all over the abdomen, and in which the diagnosis of strangulated crural hernia of the omentum was made. Operation under cocaine-adrenalin anesthesia allowed the escape of a clear yellow fluid, and the exposure of two appendices epiploicæ, measuring 2 cm. and 1.5 cm., respectively, attached by narrow pedicles to the sigmoid colon. One of these bodies was of a dark brown color; both were removed, and the patient recovered.

The other case appeared in a peasant, aged thirty-two years, who experienced a sudden attack of pain in the left inguinal region six months before observation. A month later the pain had entirely

[4] Wien. klin. Woch., vol. xviii, pp. 1367, 1368.

[5] Brucheinklemmung einer Appendix epiploica, Münch. med. Woch., 1906, liii, 16.

[6] Brucheinklemmung der appendices epiploicæ und ihre Folgen, Münch. med. Woch., 1906, ii, 1868.

disappeared; a small tumor was observed and continued to enlarge. A diagnosis of oblique external entero-epiploic inguinoscrotal hernia led to operation December 9, 1905. Incision of hernial sac and removal of omental flap; an appendix epiploica was adherent to the posterior border of neck of hernial sac and twisted about 0.5 cm. from its colonic origin. A free appendix epiploica was attached about 0.5 cm. below neck of hernial sac. The sigmoid colon was adherent to the neck of the hernial sac for about 3 cm. Removal of appendices. Recovery. The latter case proves that hernial incarceration of appendices epiploicæ may occur and disappear spontaneously, but may later result in secondary changes, such as intestinal adhesions to the neck of the sac, the formation of external hernia, or may cause rapid enlargement of an existing hernia.

To the 2 cases of hernial strangulation of appendices epiploicæ without torsion, reported by Muscatello, and a third, reported by v. Bruns, Mohr[7] contributes a fourth, which occurred in a rather fat male, aged sixty-two years, who first noticed a small, painless tumor in the region of left inguinal ring, three or four years before observation. It protruded frequently, but was always readily reduced. Recurred ten days ago; irreducible. Diagnosis of probable incarcerated omental hernia. Operation: Exposure of long delicate vermiform, free, fatty tumor, whose distal end was hypertrophied, presented hemorrhagic infiltration and was attached to posterior wall of hernial sac. The tips of two other appendices epiploicæ arising from the sigmoid colon had become strangulated at the neck of the sac and were about to undergo gangrene. They were removed. Recovery complete.

Kruger[8] reports a case in which torsion of the appendix epiploica occurred within the hernial sac. A revenue officer, somewhat stout, aged fifty-six years, gave history of pain in right groin twenty years ago, which disappeared entirely after a few weeks; recurrence two years ago. Four days before admission to hospital he had another attack, with pain radiating from urethra to umbilicus; firm tumor in inguinal region. Diagnosis: Strangulated epiplocele. Operation, May 17, 1907, revealed an appendix epiploica, 4 cm. long and 1.5 cm. wide, springing from the cecum by a short pedicle, which had passed through the inguinal canal and had become twisted in the hernial sac, giving rise to inflammatory symptoms. The pedicle was ligated about 3 cm. above the inner inguinal ring and divided; removal of appendix epiploica, hernial sac, and neck. Recovery uneventful. Krueger states that it is possible that the inflammation might have disappeared spontaneously, as it did twenty and two years previously, respectively, but the likelihood of recurrence of torsion and gangrene, followed by peritonitis, justified the radical operation.

[7] Brucheinklemmung von Appendices epiploicæ, Münch. med. Woch., 1907, liv, 170.
[8] Zur Torsion der Appendices epiploicæ, Münch. med Woch., 1907, liv, 1813.

Having briefly presented a synopsis of the cases reported in the literature, I now wish to report a case which came under my own observation, making the fifteenth case in which operation was necessary.

S., aged thirty-five years, with no history of previous abdominal trouble, was taken, at 4 A.M., September 26, 1905, with severe pain in the right iliac region. This gradually subsided, and he took the seven o'clock train for Davis, and from there drove several miles into the country. The pain increased so that he was compelled to return to Davis, where he saw Dr. Bates and received a hypodermic injection of morphine. He then took the train for Sacramento, where I saw him at 10 P.M. of the same day. The region of the appendix was painful and sensitive, and a tumor an inch and a half in diameter was distinctly palpable at the usual site of the appendix. The pulse was 80, the temperature normal. These findings remained practically unchanged until October 1, when the temperature rose to 100° F., and the operation was done. Presenting in the incision was a dense tumor about an inch and a half in length and one inch in width, having the appearance of a hematoma with a peritoneal envelop. It was universally adherent and was attached to the cecum by a narrow, rugous, and twisted pedicle. The neighboring glands were enlarged. The appendix, though seemingly normal, was removed. Recovery was uninterrupted. Macroscopic examination, combined with microscopic findings, showed the tumor to be an appendix epiploica, and the vermiform appendix to be normal.

In a study of the cases of torsion of appendices epiploicæ we find that they may be divided into two classes, intra-abdominal and hernial. Of the 15 cases reported, 7 were intra-abdominal, 8 hernial. As regards the intra-abdominal cases, in 5 of the 6 cases reported by Riedel there is no mention of torsion existing in any of the appendices at the time of operation; in 1 torsion was present; the seventh case is my own, in which torsion presented. In the 8 hernial cases, torsion was observed in 5: Riedel, 2; Muscatello, Krueger, and Lorenz, 1 each; strangulation without torsion was reported in 3 cases—Muscatello, Mohr, and von Bruns.

The intra-abdominal variety of cases may be further subdivided into (1) those in which the distal extremity of the appendix epiploica is adherent, and (2) those cases in which the distal end is loose or non-adherent. Krueger states that torsion of the appendices epiploicæ most likely results from disturbances of equilibrium, excentric development within the abdominal cavity (most cases occurring in fat persons during middle life or later) forming pedicles with hypertrophied distal ends. Circulatory disturbances, caused by progressive narrowing of the pedicle, produce inflammation of the distal extremity, which may result in adhesion to the parietal serosa, mesentery, or intestinal loops, thereby stretching

the pedicle into a still thinner band. These bands may give rise to symptoms of obstruction, due to intestinal strangulation.

When the distal portion is free the appendix epiploica may be entirely twisted off, either gradually or suddenly. In both cases free fatty bodies are formed, which may give rise to attacks of pain or peritonitis. It frequently happens that these free bodies undergo calcareous degeneration.

In the hernial group of cases appendices epiploicæ may become incarcerated in femoral or inguinal herniæ, most commonly on the left side. Of the cases reported, 7 occurred on the left, 1 on the right side. In the light forms the acute symptoms may disappear spontaneously, but it seems that the appendix epiploica remains in the hernial sac; it may be loose or it may become adherent and stretched to a thread-like thinness, or it may hypertrophy and be twisted off completely.

Strangulation of the appendix epiploica at the neck of the hernial sac, gangrene due to torsion of the pedicle, or separation of the distal portion of the appendix epiploica causes acute inflammatory conditions, which also involve the hernial sac. The pain is usually violent, frequently radiating to the hypogastrium. When the pain is referred to the back, cecal appendices are involved.

Conclusions. 1. Torsion of appendices epiploicæ is more frequent than the paucity of references in medical literature would imply.

2. Torsion of appendices epiploicæ usually occurs in persons more or less obese, during middle life and later.

3. Intra-abdominal torsion of appendices epiploicæ may simulate appendicitis, hepatic colic, cholecystitis, and various other intra-abdominal diseases. Torsion of appendices epiploicæ in the hernial sac may cause all the local symptoms of an acute omental or intestinal, femoral, or inguinal hernia.

4. Torsion of appendices epiploicæ may result in corpora aliena adiposa, in adhesions and bands, and their consequences.

5. Corpora aliena adiposa may become infected and cause general peritonitis.

6. In the present state of our knowledge anything more than a tentative diagnosis of torsion of appendices epiploicæ would be rarely possible.

7. Early operation is indicated in all cases.

PRIMARY TUMORS OF THE ADRENAL GLAND IN CHILDREN.

REPORT OF A CASE OF SIMULTANEOUS SARCOMA OF THE ADRENAL GLAND AND OF THE CRANIUM, WITH EXOPHTHALMOS.

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Tumors of the adrenal gland in childhood are not only very rare, but the histology of those that have been reported has not been, as a rule, thoroughly studied. Furthermore, they present in their clinical course differences from the adrenal growths of adults, and tend to fall into rather definite types, with clinical characteristics which may permit of an accurate diagnosis during life. For these reasons we report the following case, remarkable from both the clinical and the pathological point of view.

G. H. C., a male infant, aged sixteen months, entered the Massachusetts Charitable Eye and Ear Infirmary, September 10, 1906, in the service of Dr. Alexander Quackenboss, to whom we express our thanks for turning over the case to us for publication. The family history was excellent, the past history good up to the early part of August, 1906, when a purple discoloration of the upper and lower lids of the right eye suddenly appeared. On August 26 the child was examined by Dr. Myles Standish, who found exophthalmos of the right eye, with diffuse hemorrhagic infiltration of the upper and lower lids; the pupil unresponsive to direct light, but contracting when light was thrown into the other eye. A soft mass over the right temporal region, said to have been present two days, was noted; it measured $1\frac{1}{2}$ x 2 x 3 inches. The fundus was normal.

On entrance to the hospital the ecchymosis of the lids was very marked, with considerable protrusion of the eyeball directly forward. The latter was immobile and vision was apparently *nil;* there was no injection of the conjunctiva. A large flat swelling extended outward from the orbit to the right temporal region, reaching back as far as the ear, and involving the whole temporal region. It was smooth, rather tense, and semifluctuating, the overlying skin not adherent, but showing dilated veins. The corresponding pre-auricular lymph nodes and those at the angle of the jaw were considerably enlarged. The left eye was normal; the nose and throat, heart, lungs, and abdomen were negative on physical examination; the spleen and liver were not enlarged.

Blood examination: leukocytes, 12,000. Smears examined September 17 by Dr. W. H. Smith showed no achromia, and a differ-

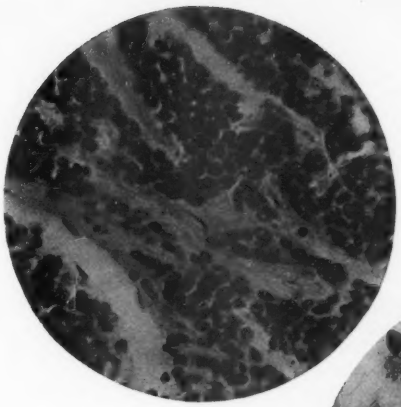
ential count as follows: polynuclear neutrophiles, 55 per cent.; mononuclears, 44.5 per cent.; eosinophiles, 0.5 per cent.

During the three weeks stay in the hospital, the exophthalmos increased slightly, the temporal growth and the metastases in the lymph nodes grew a good deal larger, and a slight ecchymosis appeared on the lower lid of the other eye. The lids on the right side had become almost black. There was slight injection of the palpebral and the ocular conjunctiva. On September 23 a small piece of the enlarged glands in front of the ear was removed for examination. It was of a bluish color (owing to hemorrhage), and was reported by the pathologist, Dr. F. H. Verhoeff, to be a small round-cell sarcoma.

FIG. 1.—Appearance of the child shortly before death.

The patient was given a careful general examination by Dr. W. H. Smith, and later by one of us (Tileston); no abdominal tumor could be made out, although one was looked for. The patient was sent home to West Springfield, New Hampshire, October 2, 1906, and was cared for there by Dr. D. P. Goodhue, to whom we owe thanks for further notes and for obtaining permission for the autopsy. The infant soon fell into a deplorable state, with almost constant pain in the region of the right eye, which almost entirely left its socket, being pushed outward, downward, and inward, so that it nearly touched the nose. The growth about the temple took on huge proportions (Fig. 1), and the cachexia increased. The patient died January 13, 1907.

Autopsy at West Springfield, N. H., thirty-two hours postmortem (Harvard Medical School Series, 3297): The body is that of an



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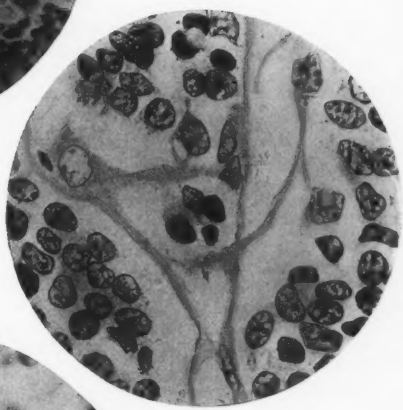

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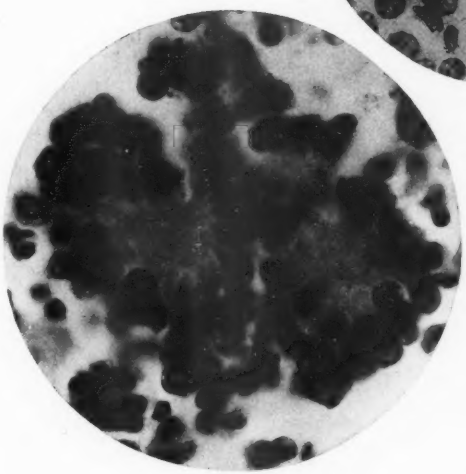

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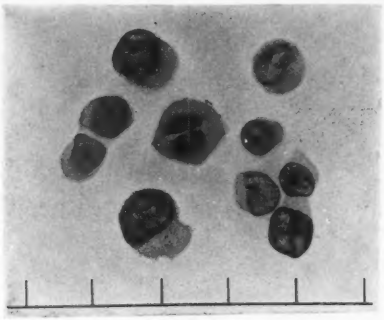
FIG. 2.—Photomicrograph of a section of the tumor, to show the general arrangement in the denser portions. (330 diameters.)

FIG. 3.—Drawing reduced from fifteen hundred diameters, to show the reticular supporting tissue.

FIG. 4.—Photomicrograph of two rosettes. (660 diameters.)



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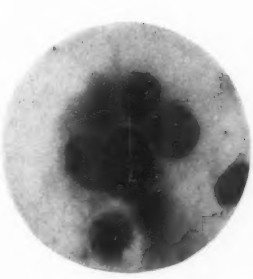

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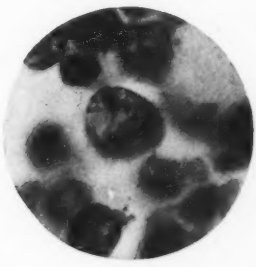

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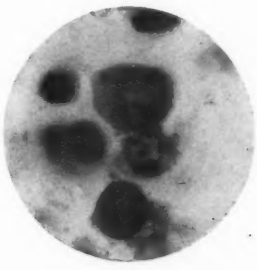

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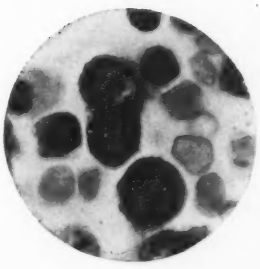

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FIG. 5.—Drawing of single tumor cells, showing the variation in size and also a cell in mitosis. Each division of the scale equals ten microns.

FIGS. 6, 7, 8.—Photomicrographs of tumor cells, showing details under high power for comparison with Figs. 5 and 9. (1140 diameters.)

FIG. 9.—Photomicrograph of myelocytes from the erythroblastic liver of an infant. From a case of severe anemia with splenomegaly.

emaciated, poorly developed male infant, 79 cm. long. There is no rosary. The head is greatly deformed and turned to the right. There is marked œdema of lower limbs, penis, and scrotum. The legs are covered with numerous, small, red areas which do not disappear upon pressure. There is a large decubitus on the right hip, exposing the great trochanter, which is denuded of periosteum; and a small decubitus upon the back at the costal angle below the left scapula. There are prominent lymph nodes on the right side of the neck, at the angle of the jaw, and along the sternomastoid muscle; the lymph nodes elsewhere are not palpable.

The deformity of the head is due chiefly to a huge tumor mass on the right side, covering the forehead and frontal bone, and producing great prominence of the zygoma, which is freely movable and pushed forward and downward. The right eye is pushed forward and is directed inward; the sclera is loose; the cornea is clouded. The alveolar process of the superior maxilla is asymmetrical, presenting a greater convexity on the right side. The buccal surface of the palate is convex. The general contour of the right side of the face is convex, due to a diffuse tumor, involving the parotid region as well as the parts described above. There is marked œdema of the scalp and face on the right side. Over the right inferior occipitoparietal angle is a large, rounded, boggy eminence about 11 cm. in diameter. The whole right side of the scalp and face is dark reddish blue in color. The consistency of the tumor over the forehead is soft and elastic, not fluctuating. The following measurements were taken: circumference of head, at level of left frontal eminence 53 cm.; from anterior fontanelle to symphysis of inferior maxilla, right side, 27.5 cm.; left side, 22 cm.; from external auditory meatus to midline, determined by the teeth, right side, 13 cm.; left side, 9.5 cm.

There is no subcutaneous fat and no fat in the omentum, mesentery, and about the kidneys. The omentum is thickly sprinkled with small black dots and irregular black areas, without thickening (old hemorrhages). The peritoneal surfaces are everywhere smooth, moist, and glistening. The colon is inflated in some places; in others contracted and injected about hardened masses of feces. The mesenteric glands are not remarkable. The appendix is normal. The diaphragm reaches to the fourth rib, left; third interspace, right. In the right side of the abdomen, behind the ascending colon, and compressing the kidney and pushing up upon the liver, is an irregular, soft, elastic tumor mass. The shape is roughly that of a flattened ovoid with a broad lateral process crossing the spine. The posterior portion of the right lobe of the liver is flattened horizontally, and is adherent to the tumor. The right kidney is flattened to one-half of its normal thickness, as far down as the junction of the lower and middle thirds. The lower border of the tumor is at the level of the middle of the fifth lumbar vertebra. The inferior vena cava runs through the anterior portion of the tumor, 0.5 cm. below the anterior

surface, and lies 4 cm. to the right of the spine and 1 cm. anterior to its normal position; it is flattened and completely surrounded by the tumor mass, as far down as the point where it is crossed by the common iliac artery. In the upper portion of the vena cava just before it leaves the tumor, there is a small flattened, mural thrombus of friable, grayish red clot. The lower portion of the tumor crosses the spine, and lies upon the aorta and pelvis of the left kidney, and compresses both of these structures. The tumor is not adherent to either kidney, and all surfaces are invested with a thin, fibrous capsule. The dimensions of the tumor, measured in situ, are: Vertical diameter, 12 cm.; transverse diameter along the lower portion, 8 cm.; anteroposterior diameter, 8 cm. On section, the tumor is made up of spherical masses of pale, translucent, grayish, soft, elastic tissue, with large areas of hemorrhage and necrosis. In the upper portion the adrenal gland is included. The superior border of the adrenal is intact; the medulla of the bulk of the gland is continuous with the tumor tissue, while the cortex of the lower part diverges to include a dark red, spherical mass, 1 cm. in diameter, and is then gradually lost in the tumor tissue, running for some distance as faint yellow lines. The compressed portion of the liver is not invaded by the tumor. There are several smaller spherical and flattened spherical masses, 1 to 2 cm. in diameter, attached to the various surfaces of the larger tumor. These on section prove to be continuous with the main tumor body, while the external surfaces are covered with a thin, smooth, fibrous membrane.

The pleural cavities are normal; no free liquid; no adhesions. The thymus gland is small; estimated weight, 1.5 grams. The pericardial cavity is normal and the heart is normal in size. The myocardium is of good color and consistency. The valves and endocardium are normal. The foramen ovale is closed. The lungs are uniformly soft, pale, and downy, with the exception of narrow lines of postmortem settling on posterior borders. Bronchial nodes not remarkable.

The spleen is large; length, 6 cm.; breadth, 4 cm. The proportions are normal, and the capsule is smooth. The color and consistency are normal. The liver is 13 cm. in breadth; antero-posterior diameter of right lobe is 9 cm. The posterior portion of the right lobe is compressed by the abdominal tumor described. The color and consistency are normal. The gall-bladder and ducts are normal. The gastro-intestinal tract is normal except for small areas of injection in the colon, in portions contracted about hardened feces.

The pelves of both kidneys are much dilated and contain numerous soft, brownish masses of granular material. Both kidneys smooth non-adherent capsules. The color is normal. The glomeruli are visible. The upper ends of both ureters are slightly dilated. The right kidney has a concave anterior surface, corresponding to the

upper two-thirds which was in contact with the tumor mass in the abdomen. This portion of the kidney is about one-half the thickness of the lower third, and slightly broader.

The pancreas, bladder, testicles, and thoracic duct are normal.

The organs of the neck are normal. There is a large mass of soft pink and deep red glands at the angle of the jaw. Those along the sternomastoid are firm, large, and gray.

The femur, vertebræ, sternum, and ribs are normal. All contain red marrow.

The hair of the head is short and sparse; dark-brown. The scalp and skin are much thinned on the right side of the face. The scalp is markedly œdematous, particularly over the right lower occipitoparietal angle. Beneath the aponeurosis of the whole frontal regions is a soft elastic tumor mass, deepest just below the frontal eminence, where it is 5 cm. deep. Superiorly and laterally the mass gradually diminishes in depth. Inferiorly it is continuous with the tumor tissue on the side of the face and behind the zygoma. The right parietal bone slightly overrides the left, and the parietal suture is studded with small, soft, reddish elevations. The anterior fontanelle is 1 cm. in diameter. On removal of the calvarium, a large, extradural tumor mass is found to fill the whole anterior fossa of the skull. This tumor mass is 6 to 7 cm. deep, and is continuous with the tumor mass on the external surface, through an opening in the frontal bone directly over the orbit. The opening, as near as can be determined, is 2 to 3 cm. in diameter. The adjacent bone is covered on all sides and both surfaces with necrotic and hemorrhagic tumor tissue, and sends innumerable delicate bony spicules into the substance of the tumor. The whole of the tumor within the skull is dark red, in places very soft and necrotic. The orbital plate on the right side is elevated and eroded. All of the accessory sinuses, the antrum of Highmore, and the nasal cavity are filled with dark red, soft, tumor tissue. The internal surface of the dura over the vertex is thickly studded with soft, translucent, grayish nodules, 1 to 3 mm. in diameter. The dural sinuses are normal. The tumor superiorly extends backward between the dura and bone within the skull as far as the lambdoidal suture. On the left side it extends 2 to 3 cm. beyond the median line. The left orbital plate is recessed, and the posterior part of the orbit contains tumor tissue. The pituitary body cannot be found. There is marked deformity of the floor of the skull; the basilar process of the occipital bone is directed inward to the left. The sella turcica is flattened. The general shape of the skull is that of a distorted ovoid, inclining toward the right.

There is marked asymmetry of the brain. The right half of the frontal region slopes obliquely toward the left; the frontal lobe is flattened, as far back as 2 cm. from the tip of the temporal lobe. Both tips of the frontal lobes are flattened and slope obliquely upward

The olfactory processes are small, flattened, and lie parallel with the median fissure, which is directed toward the left. The pia is normal. The convolutions are slightly flattened over the regions already indicated. Elsewhere there is no flattening. The consistency of the brain is moist and soft (postmortem?). Nothing abnormal is found on section of the hemispheres, pons, basal ganglia, medulla, and cerebellum. The vessels at the base are normal.

Anatomical Diagnosis. Sarcoma of the cranial cavity; sarcoma of the right adrenal; emaciation; deformity of the skull and brain, due to a growth under pressure; œdema of the lower extremities due to pressure on the abdominal vessels; mural thrombus of the inferior vena cava.

Microscopic Examination. The following stains were used after Zenker fixation: methylene blue and eosin; Mallory's connective tissue stain; and Mallory's phosphotungstic acid hemotoxylin stain.

Portions of the mesentery containing the dark spots, when treated with potassium ferrocyanide and hydrochloric acid, give the reaction for iron-containing pigment.

The heart, liver, pancreas, adrenal, testicle, and mesenteric lymph nodes are negative.

Spleen. The corpuscles are of good size, symmetrical and abundant, but contain few active cells. The pulp is moderately injected. Both pulp and corpuscles contain numerous polymorphonuclear eosinophiles. A large lymphatic accompanying a branch of the splenic artery at the hilum is tightly packed with small round cells, which on one side are invading the surrounding connective tissue. These cells have round or oval nuclei 5 to 8 microns in diameter. The nuclei stain deeply with the basic stain, and have a coarse basic-staining reticulum, usually with a large chromatin mass at the centre and other smaller masses scattered throughout. The protoplasm cannot always be made out. In places it occurs as a narrow, pinkish, finely granular, eccentric band, without a membrane.

Kidney. The cells of the convoluted tubules are swollen and granular. There are numerous hyaline casts in the collecting and Henle tubules. There are many imperfectly developed glomeruli.

Thymus. The lobules are very small and contain much hyaline connective tissue. The epithelial rests are very small and completely converted into hyaline-like material. There are very few cells resembling lymphoid cells, and the bulk of the cells are spindle-shaped connective tissue cells.

Cerebrum. Temporal Lobe. There is apparently an increase of cells resembling the satellite cells throughout the cortex. The ganglion cells are small; they are usually surrounded by a clear space. The protoplasm is broken up into groups of granular material, and the nuclei are surrounded by clear spaces, so that the cell outlines are indicated by rather narrow fringes of granular protoplasm (postmortem change?). No Nissl granulations are visible. A few gan-

glion cells contain minute rings of eosin-staining material. The nuclei are deeply stained with the blue; a few are large and vesicular.

Tumor. The arrangement is that of closely packed, small, round cells, supported by a delicate connective tissue reticulum. In places the cell groups are divided by the reticulum into round or irregular and elongated masses (Figs. 2 and 3). In many places the cells are arranged two to four deep in rosette form about masses of eosin-staining, finely granular material; the groups vary from 20 to 70 microns in diameter. This rosette arrangement occurs in all the sections taken from different parts of the growth, in the abdomen, glands, upon the dura, and in the head (Fig. 4). Where the tumor is invading the frontal muscle and adrenal this arrangement ment does not occur. The abdominal mass has completely surrounded the adrenal, and has destroyed the major portion of it, apparently by pressure, as the capsule and cortex are invaded in only a few places. Dilated lymphatics of the adrenal capsule are filled with tumor cells. In some places there is a definite invasion of the cortex with disappearance of the capsule. A lymph node from the angle of the jaw is completely filled with tumor masses, large hemorrhagic foci, and necrotic cells. Here the arrangement is chiefly in rosettes. The reticular structure of the lymph node is present only in places.

Everywhere throughout sections of the tumor from all locations, there is much necrosis of the tumor cells, resulting in hyaline eosin-staining bodies containing one or several irregular-shaped basic-staining granules. The tumor cells are about the size of the largest myelocytes found in erythroblastic centres in bone marrow (Figs. 5, 6, 7, and 8). The nuclei are 5 to 8 microns in diameter. There is very little protoplasm, often none is demonstrable. Usually the protoplasm is eccentrically arranged. It stains purplish, is finely granular, and has no cell membrane, nor granular inclusions. Often the cells of the rosette groups are elongated; the protoplasm is drawn out radially on the central side of the nucleus. Occasionally the nucleus is egg-shaped, with the small end toward the centre of the group. The nuclei, as a rule, are round or oval, and vesicular in appearance. A few show peripherally arranged chromatin masses, but the general distribution of chromatin is a scattered one throughout the nucleus. There is usually a central basic-staining round mass, larger than the scattered chromatin material. The nuclear reticulum is coarsely meshed and very prominent. A few mitotic cells are found. There is evidence of direct nuclear division in the shapes assumed by large nuclei, and the frequent presence of two nuclei in one cell.

The phosphotungstic acid hematoxylin stain reveals no fibrils connected with the tumor cells.

The cells undergoing mitosis are a trifle larger than the other tumor cells; the one illustrated is 10 microns in diameter. The

protoplasm is a purplish pink and finely granular. At the periphery of the protoplasm there are usually numerous, small, deeply stained basic granules (Fig. 5). In all portions of the tumor there are many cells with perfectly definite, abundant, coarsely granular protoplasm, with nuclei which are small, densely colored with the basic stain, and separated from the protoplasm by a narrow, sharply demarcated, unstained space. These are probably degenerated cells (Figs. 6, 7, and 8). The reticulum consists of a delicate fibrillar connective tissue, accompanied by large cells resembling those of embryonic connective tissue (Fig. 3).

In all sections of the tumor which include adjacent normal tissues, the veins and lymphatics of the latter contain clumps and often rosettes of tumor cells. In the dura there are tumor cells in the veins, from which invasion of the tissues is apparently taking place.

The marrow from the femur shows normal active marrow, with many small groups of tumor cells, ranging in size from closely packed groups of six to ten cells, to masses 1 mm. in diameter, showing the characteristc groupings and type of cells occurring elsewhere in the tumor.

Summary and Classification of the Tumor. In this case the striking pathological feature is the finding of large identical tumors in the abdomen, involving only the adrenal, and in the cranium, involving only adjacent soft tissue and lymph glands. In spite of the frequent finding of tumor cells in the bloodvessels and lymphatics, metastases were found only in the bone marrow and the lymph nodes of the neck. The slight tendency to invasion is shown by the presence of a large portion of intact adrenal in the abdominal tumor mass, and in the flattening of the liver and kidney, without extension into either. The tumor is a small round-cell sarcoma. belonging to the type in which the cells are supported by a reticulum. The cells resemble the undifferentiated cells of the bone marrow.

In the classification of this tumor, it should unquestionably be placed in that group of tumors which includes all those derived from the blood-forming cells, both white and red. Ribbert has proposed the name lymphocytoma for this group, which includes all those tumors called malignant lymphoma (lymphosarcoma, malignant lymphadenoma, etc.), chloroma, myeloma, and possibly the leukemias. The essential features of this group are the reticular supporting tissue, and the type of tumor cell, which represents a more or less incompletely differentiated cell belonging to the blood forming series.

Two characteristic tumors of this group present cells in which the type is readily recognizable; the myeloma, in which the cells resemble very closely certain cells found normally in the bone marrow and probably identical with plasma cells, and the lymphoma, in which

the cells resemble either differentiated lymphoid cells, or the cells of the germinal centres of lymph follicles.

The peculiar grouping of the tumor cells in rosette arrangement, shown in Fig. 4, deserves consideration. Unlike other tumors in which there is a rosette arrangement, certain gliomas, for instance, there is no attempt at lumen formation. In no instance could vessels or connective tissue, or remains of either, be found in the centres of these groups. The examination of many sections has proved the shape of these clumps of cells to be roughly spherical or ovoid, thus excluding the possibility of columnar growth about a supporting tissue, which in cross section might give such an appearance.

While these rosettes are found in all portions of the tumor, they are most common in those parts where there is least supporting tissue, and are found even in the metastatic masses of cells within bloodvessels. The possibility of an agglutinative phenomenon is perhaps worthy of mention, because of the suggestion that the cells, in the absence of a supporting tissue and because of the very soft consistency of these portions of the tumor, were suspended in a liquid or semiliquid medium. This is also suggested by the presence of a very fine granular deposit, which stains lightly with eosin, resembling that thrown down by Zenker's fixative from liquids containing albumin. The granular central substance of these clumps can also be explained by this hypothesis, while it is otherwise difficult to account for it, because in the absence of nuclear remains, it is not probable that it is derived through the degeneration of cells.

Another perhaps more plausible explanation is that the tumor cells, after multiplication, have failed to separate from one another, and by their cohesion produced the rosette arrangement. Until a number of tumors similar to this one have been accurately described it is best not to attempt to select a descriptive name.

For clinical purposes, tumors of the adrenal gland in children may be divided into four classes: (1) Those with metastases to the skull (Hutchison's type); (2) those of simultaneous sarcoma of the liver and adrenal; (3) those associated with precocious maturity; and (4) those not falling under any of the preceding headings.

It is in connection with the first of these types that the foregoing case is important. Hutchison has recently called attention to this new clinical syndrome, and has reported 10 cases, 6 hitherto unpublished, and 4 from the literature. In view of the rarity and great interest of this condition, it has seemed desirable to collect and analyze as many cases as possible. We have reviewed the literature carefully, and have succeeded in adding 4 new cases to the list, while we have left out one of those included by Hutchison (that of Ogden and Mathews), for reasons that will be given later. This

brings the total number of cases reported up to the present time, including our own, to 14.

The following description applies to Hutchison's type of adrenal tumor (the others will be considered later). This syndrome has been found hitherto only in infants or young children, and shows the following characteristics: Spontaneously or after trauma there appears ecchymosis of one or more eyelids, soon followed by exophthalmos, which is usually one-sided. The eye becomes more and more protruded, and there appears a growth in the adjacent temporal region, with enlargement of the lymph nodes in front of the ear and at the angle of the jaw. A tumor in the region of the kidney is felt during life in the minority of cases (6 out of 14); most frequently, as in our case, it constitutes one of the surprises of the postmortem table. The orbital tumor grows with great rapidity, and death ensues early from cachexia and anemia. Optic neuritis may occur, but total blindness is the exception. Pain in the head is frequent, but vomiting, in spite of the extension inward toward the brain, is rare. The abdominal growth may be quite large, and is then accompanied by swelling of the superficial abdominal veins, but never by ascites. Fever is usually absent. The urine, in the few instances in which it has been examined, has been free from blood and albumin, except in Aisenstein's case, in which albuminuria was present. The blood shows a secondary anemia, which may become extreme; there was reduction of the red cells to 1,400,000 in one case. The white cells are not increased, but there is usually a relative decrease of the polynuclear neutrophiles; whether the increase in basophiles affects the lymphocytes or the cells probably originating in the bone marrow (pre-myelocytes and allied forms) does not appear from the details reported, polynuclears only being mentioned.

The early age of the patients deserves especial emphasis. Twelve of the 14 were not over three years of age; 4 were under one year; 2 between one and two years; 6 between two and three years; only 2 were over three years; the eldest being nearly nine years old. The male sex predominated, with 9 boys to 4 girls (the sex is not stated in one case).

Pathological Anatomy. The adrenal growth varies from the size of a walnut to that of a child's head. It is usually one-sided, the right and the left side being involved with almost equal frequency. On section the surface is smooth, gray-white or yellow, and mottled with hemorrhages. There is little tendency to invade the neighboring tissues and organs. Metastases to the calvarium were present in all cases, to the ribs in 4, to the spine and tibia in 1 each; in 1 case the bone marrow and periosteum of several of the long bones were involved. In this connection it is interesting to note that of the cases of primary adrenal growths in children in the literature, in which the cranium was not involved, not one showed metastases to

other bones, with the exception of Caillé's[1] case, which is incompletely reported. In Cohn's case, besides the cranial growths, almost all the ribs showed metastases at the junction with the costal cartilages, presenting a picture like that of rickets, and as he points out, the great vascularity and rapid growth of these parts in infants may well be the reason for the preference shown to the skull and ribs in both diseases. In spite of the large size of the growths in the skull, the brain is not invaded. Of other organs, the liver, kidneys, and lymph nodes were most often the seat of metastases; the ovaries once.

Histology. These tumors are almost invariably sarcomas; in 3 cases only was another diagnosis made, that is, hypernephroma twice, and melanotic carcinoma. Five of the 14 showed practically the same structure, being classed either as small round-cell sarcoma (3 cases), or as lymphosarcoma (2 cases). Three are described as "round and oval-cell sarcoma," 1 as "medullary sarcoma," and 1 simply as "sarcoma." One case is reported without microscopic examination.

In view of the rarity of the condition, we shall give a brief description of the cases hitherto reported, in chronological order. The 6 original cases of Hutchison are designated by the numbers they bear in his table.

Case I. Cohn. Female child, aged nine months. First symptoms, "boil" on the right temple and exophthalmos of the right eye; soft semifluctuant flat tumor in the right temporal region attached to the bone; five similar smaller tumors behind the left ear; deep in the right flank a tumor not connected with the liver; spleen and liver enlarged; no blood or albumin in the urine; tremendously rapid growth of the cranial and abdominal tumors; great enlargement of the occipital and deep cervical lymph nodes; no fever; death in five weeks. At autopsy a large tumor of the right adrenal, with secondary nodules in the right kidney, liver, ovaries, and most of the ribs at the junction with the costal cartilages. Virchow diagnosticated "medullary sarcoma," primary in the adrenal.

Case II. Reimann. Female infant, aged three months at the onset; first symptom, subcutaneous nodules of a bluish color; these did not increase in size, but fresh ones continually appeared; no exophthalmos, but two small periosteal tumors on the parietal bones; death at the age of seven months. At autopsy primary tumors of both adrenals, very numerous metastases in the bones, subcutaneous tissues, muscles, dura mater, and liver; metastases in both parietal bones, in the marrow of the long bones, and also in the periosteum of these bones. Chiari made the diagnosis of melanotic carcinoma; microscopically the tumor consisted of round and

[1] Archives of Pediatrics, 1895, xii, 594.

"epithelioid" cells arranged in islands separated by connective-tissue septa, and bearing large masses of granular pigment.

CASE III. Barnard (Case V of Hutchison). Boy aged two and one-half years; fall on the head six weeks previously; next day cheek and eyes swelled; on examination entire head enlarged, both eyes forced out of their sockets, soft tumor masses on the forehead; in the left hypochondrium an irregular tumor lying deeply, with the intestine in front of it. Red cells, 3,200,000; whites, 8400; polynuclears, 47 per cent. The correct diagnosis was made during life; at autopsy sarcoma of the left adrenal, infiltration of the calvarium with newgrowth, a small metastasis in the liver.

CASE IV. Aisenstein. Boy, aged two years. First symptoms, anemia, loss of weight, pain on walking or standing. Fever throughout the disease. Albuminuria, dulness in chest due to enlarged mediastinal glands. A month after admission hemorrhage into left eyelid. Hemorrhagic pleural effusion. Lateral displacement of lower dorsal vertebræ. Finally large tumor on frontal bone, large deep-seated mass in region of stomach, small scattered round tumors in abdomen. Marked anemia; death at the end of three and one-half months. Clinical diagnosis, tuberculosis. At autopsy large tumor of left adrenal, with numerous metastases to the skull and ribs, also to the abdominal, mediastinal, and cervical lymph nodes, and to the pancreas. Microscopically oval and polygonal cells with alveolar arrangement; the tumor is classified as an alveolar sarcoma or endothelioma, belonging to the hypernephroma group.

CASE V. Bruck. Female, aged one year and two months; first symptom pain in the abdomen with swelling, then discoloration and swelling of the right eyelid; no exophthalmos. Tumor of the liver reaching nearly to the anterior superior spine of the ileum. Exploratory operation; death the same day. At autopsy a tumor of the right lobe of the liver the size of a child's head, and of the right adrenal the size of an apple; smaller tumors on the upper wall of the orbit, and in the dura of the frontal bone. Tumors of liver and adrenal not continuous; pancreas involved by extension. Microscopic examination, small round-cell sarcoma.

CASE VI. MacCarty. Child (sex?), aged two and one-half years. Eight weeks before entrance to the hospital a small "boil" on the left side of the head. Soon after, right exophthalmos, enlarged glands behind the ear and in the left axilla; abdomen distended. A small tumor in the jaw appeared, following the extraction of a tooth. On examination a fluctuant tumor the size of a large apple in the left parietal region; a smaller tumor in the left axilla; right exophthalmos; liver three fingers' breadth below the ribs; spleen palpable. Blood: polynuclears, 70 per cent.; lymphocytes, 27 per cent.; eosinophiles, 3 per cent. Anemia; no nucleated red cells, some macrocytes and poikilocytes. Fever throughout the course of the disease, death in ten weeks. At autopsy a tumor of the right

adrenal the size of a child's head; diagnosis, "malignant hypernephroma." Four metastases in the cranium, one very large, with complete erosion of the bone; metastasis in the axilla.

CASE VII. Richards (Case XXX of Richards' series). Male, aged six months. At the age of two months a lump appeared at the posterior fontanelle, and reached the size of a small orange; a similar tumor destroyed the right eye. Tumors also in the arm and leg. The autopsy showed three tumors of the calvarium, projecting both inward and outward, and covered with a thin shell of bone; other metastases in the fifth and sixth ribs, bronchial glands, liver, subcutaneous and muscular tissues of the arm and leg. Primary tumors 4 x 3 inches in both adrenals; histologically small round-cell sarcoma.

CASE VIII. Hutchison (I). Boy, aged eight years and nine months. Ecchymosis of left eye, headache and vomiting since a blow on the forehead five months before admission. Left cervical glands enlarged. A tumor in the left loin. The left eye later became protruded and the cornea destroyed. Tumor on the left tibia. Death in six months from onset. Autopsy: large tumor involving left kidney and left adrenal; calvarium infiltrated with growth. No secondary deposits elsewhere.

CASE IX. Hutchison (II). Boy, aged ten months. Swellings on the head first symptom; left eye protruded; hemorrhage into the orbit; provisional diagnosis scurvy. Died soon after admission. Reds, 3,125,000; whites, 12,000; no abnormal white cells. Autopsy: small round-cell sarcoma of the medulla of the left adrenal; calvarium and cervical glands infiltrated. No secondary deposits elsewhere.

CASE X. Hutchison (III). Boy, aged two and one-half years. Lumps noticed on the head five months before admission. Tumors of the forehead and temporal fossæ, ecchymosis and protrusion of the right eye-ball. The liver enlarged. Died six weeks after admission. Reds, 1,572,000; hemoglobin, 45 per cent.; whites, 14,500; polynuclears, 31 per cent. Autopsy: the right adrenal contained a tumor the size of a walnut. Secondary nodules in the liver and cervical glands; extensive growths in the calvarium and base of the skull. Microscopically, round- and oval-cell sarcoma.

CASE XI. Hutchison (IV). Girl, aged four years. Pains in the limbs and head for six months; great weakness. Tumor in the left hypochondrium. After admission optic neuritis, lumps on the forehead, and left-sided exophthalmos. Died three and one-half months after admission. Reds, 3,942,000; hemoglobin, 70 per cent.; whites, 10,500; polynuclears, 51 per cent. Autopsy: large nodular growth of the left adrenal, deposits in the lymph nodes all over the body, in the bones of the skull, and on the inner aspects of all the ribs but the first. The growth consisted of round and oval cells; the diagnosis was sarcoma or papilloma.

CASE XII. Hutchison (VI). Boy, aged three years. Ill two weeks, but pale for a considerable time. Hemorrhage from the gums. Growth in the left temporal fossa, slight exophthalmos. Optic neuritis, blindness. No tumor felt in the abdomen. Urine normal. Died nine weeks after the onset. Reds, 1,400,000; hemoglobin, 35 per cent.; whites, 8000; polynuclears, 65 per cent. Autopsy: sarcoma of the medulla of the left adrenal; infiltration of the calvarium and thoracic spine. Microscopically, round and oval-cell sarcoma.

CASE XIII. Hutchison (X). Boy, aged three years. Blackening of the left eye four weeks before admission; no history of injury. Double exophthalmos; both upper lids blackish; hemorrhage into the left conjunctiva. Ovoid elastic tumor on the right parietal bone and a rounded prominence above the right ear. Profound anemia. Spleen palpable. Urine normal. The abdomen became tender, but no tumor was felt. Died four weeks after admission. Autopsy: large tumor of left adrenal; the entire surface of the skull covered by huge masses of newgrowth, containing spicules of bone; invasion of both orbits. No deposits elsewhere. Microscopically, lymphosarcoma.

We have left out the case of Ogden and Mathews,[2] included by Hutchison in his table, on the ground that the adrenal origin, although probable, was not certain. The cranial metastases were, to be sure, quite characteristic, but the abdominal growth consisted of a large retroperitoneal mass involving the liver and upper pole of the kidney, no mention being made of the adrenal gland. Although this case, as well as those of Moreau[3] and Oshima,[4] may well have been of adrenal origin, the proof is lacking, and we believe it to be safer, in seeking to establish a new clinical syndrome, to keep to well established instances.

Reimann's case differs somewhat markedly from the others, both in the presence of melanotic pigment, and in the multiplicity and small size of the metastases. The diagnosis of carcinoma is open to question, such growths being more usually styled sarcomas, but the histological details are not complete enough to admit of exact classification. We have included it because the primary tumor was in the adrenal gland, and metastases to the skull were present, although small and not located in the orbit.

After this review of the literature, the question as to which of the tumors in our case was primary can be considered to better advantage. The identical histological appearances render it certain that all were of the same nature. The primary seat, however, cannot be decided from the gross or microscopic picture, for the cranial and abdominal tumors were both large, and the tumor cells showed no

[2] Brit. Jour. Childr. Dis., 1906, iii, 394.
[3] Bull. de la Soc. Anat. de Paris, 1852, 239.
[4] Wien. klin. Woch., January 24, 1907, 93.

resemblance to adrenal tissue. It is well known, however, that a small tumor may give rise to enormous metastases, and in view of the inaccessible position of the adrenal, the failure to palpate the tumor during life is of no importance. Several lines of argument, nevertheless, lead us to regard the adrenal tumor as the primary one.

In the first place, we have been unable to find instances in which a primary tumor of the cranium has caused metastases to the adrenal gland; and enlargement of the pre-auricular glands, so constantly met with in the group of cases under consideration, is exceptional in sarcoma of the orbit.[5]

Another point in favor of the adrenal origin is the well-known predilection of adrenal tumors to metastasize in the bones. This is especially true of the hypernephromas of adults, of which Scudder, in 1907, collected 17 instances with bone metastasis, to which we have been able to add 34 more, bringing the total up to 51. The great frequency of bone metastases in these tumors is even better brought out by a study of the cases followed to autopsy; thus, Albrecht found them present in 5 out of 11, and Böhler in 5 out of 10 autopsies. The relative frequency of bone metastases is, therefore, probably greater in the case of adrenal growths than in tumors of any other organ. The hypernephroma of adults, however, rarely causes exophthalmos, the metastases being situated in the skull fairly often, but almost never in the orbit (1 case of the 51 with bone metastases).

It would not do, however, to lay too much emphasis on the occurrence of bone metastases in hypernephroma, for this type of tumor shows a structure resembling that of the adrenal gland, and the group in question does not. It is very possible that the frequency of bone metastases might be because of the nature of the growth, not because of the location. For tumors of the lymphocytic series have a tendency to metastasize in tissues of a similar nature, that is, in the bone marrow and lymphoid structures. And the cells of the tumor in our own case resemble closely the myelocytes found in erythroblastic centres in bone marrow.

The final argument is derived from a critical study of the cases in the literature. No less than six, or almost one-half (Cases VI, VIII, IX, XI, XII, and XIII), show involvement only of the adrenal, the bones, and the lymph nodes. If it were assumed that the orbital tumor was the primary one, it would surely be very remarkable that it should in so many instances give metastases only to the suprarenal gland of all the viscera, whereas in the case of one form of adrenal tumor, the hypernephroma, solitary metastasis to the bony system is well established. Furthermore, in Richards' case both adrenals were the seat of tumors, which again would be exceptional on the

[5] Cf. Lagrange, Tumeurs de l'œil et de l'orbite., Paris, 1904, vol. ii.

assumption of metastasis, while the involvement of both glands in primary growths is not uncommon.

We, therefore, regard the adrenal tumor as primary in our case, which resembles closely those hitherto reported; Case XIII, in fact, appears identical with ours in every respect.

It remains to give a brief consideration of the other forms of adrenal tumor occurring in children. The second type, already referred to, is that of simultaneous sarcoma of the liver and adrenal. It has been well described by Pepper, and is met with as a congenital tumor in the first weeks of life; clinically there is enormous enlargement of the liver, without ascites, and, as a rule, without jaundice. The liver is sometimes involved alone, usually in company with the adrenal. Histologically there is in all instances a diffuse infiltration with small round-cell sarcoma.

The third type is extremely interesting with regard to the relation of the adrenal glands to the growth of the body, and to sexual development. The disease is chiefly seen in girls of one to eight years of age, and runs a comparatively slow course, usually of several years' duration. These children present a very remarkable appearance, the face and pubes being covered with an abundant growth of hair, and the external genitalia as fully developed as in the adult. They are obese and abnormally large for their age, a child of five years having the size and general appearance of a boy of sixteen (Linser's case). Pigmentation of the skin may occur, but the color is more like that of a brunette or gypsy than like the bronzing seen in Addison's disease. The intellect is dulled and the disposition sullen. Appetite, and sometimes thirst, are increased, and vomiting is likely to be an obstinate feature. The urine may contain albumin, due to the presence of blood, but sugar is absent. At autopsy a tumor of the adrenal gland is found, which is usually large, reaching up to 3 pounds (Fox's case).

Almost all of these tumors which have been examined histologically have shown a structure more or less resembling that of the normal adrenal gland, and, therefore, come into the group of the hypernephromas. This is important, as indicating the possibility of an increased adrenal secretion in these cases. And, indeed, in three instances (Otto,[6] Crecchio,[7] Marchand,[8]) premature development has been associated with simple hyperplasia of the adrenal glands.

Either precocious maturity, or giant growth, or both, have been found also in tumors of the pituitary and pineal glands, of the testes and ovaries; and retardation of growth has been associated with lack of development of the thyroid (cretinism), and of the adrenal

[6] Path. Anat. Beobacht., 1816, 139. Quoted by Lancereaux. Dict. Encycl. d. Sciences Méd.

[7] Wien. med. Presse, 1866, Nr. 30, p. 763.

[8] Internat. Beiträge zur Wiss. Med., 1891, Band i. Festschrift f. Rudolf Virchow, p. 554.

glands. For this and other reasons all these glands may be assumed to have an intimate physiological connection with one another (Linser). Lack of space, however, forbids a further discussion of this interesting subject, fully dealt with in the articles of Linser, and Bullock and Sequeira, to which the reader is referred.

Other tumors of the adrenal (Group IV) occur in children, but they show no distinctive clinical features, and, therefore, do not require a detailed consideration here. Sarcoma, carcinoma, glioma, and hypernephroma without precocious maturity, have all been observed. Rachmaninow[9] has reported several cases of mixed tumors of the adrenal, but the kidney was involved in all, so that they are more properly to be classified with the "congenital adenosarcoma of the kidney" described by Birch-Hirschfeld.

DIAGNOSIS. Tumors of the orbit in infants and young children should arouse the suspicion of metastases from an adrenal growth, and the abdomen should be carefully palpated; an abdominal tumor if present is almost sure to be of adrenal origin; the presence of enlarged pre-auricular glands renders primary sarcoma of the orbit unlikely. Chloroma presents almost identical growths, being associated with tumors of the orbit in two-thirds of the cases, with exophthalmos usually as the first symptom. It may be excluded by the absence of leukemic changes in the blood. Myeloma may cause bony growths about the skull, but is exceedingly rare in childhood; the presence of the Bence-Jones body in the urine would render the diagnosis of myeloma certain, while its absence is not conclusive.

An abdominal tumor associated with precocious maturity is practically certain to be of adrenal origin, if tumors of the ovaries or of a retained testis can be excluded. Other adrenal tumors in most cases cannot be distinguished from tumors of the adjacent tissues, especially of the kidney.

TREATMENT. The only hope lies in early radical removal, but unfortunately these tumors usually pass unnoticed until either their great size or the presence of metastases attracts attention, and then it is too late, as a rule, for a successful operation.

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CONGENITAL ABSENCE OF THE GALL-BLADDER.

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Mrs. M. was admitted to the Columbian Hospital July 19, 1907, with the following history: She was fifty-four years of age, had been sick from time to time during the past five years, and had a severe attack of typhoid fever ten years ago. At the beginning of her present illness she had symptoms of gastric ulcer. The gastric pain subsided, and later she had well-marked discoloration of her skin and other evidence of obstruction of her bile-ducts. Her appearance indicated poor nutrition, with marked anemia, and evident mischief about the gall-bladder or bile-ducts. On examination a mass could easily be outlined; this was thought to be the gall-bladder, and we were confident that several stones would be found. Operation was done on July 20, and the following conditions were observed: The gall-bladder was conspicuously absent, and the duodenum and pylorus were elevated and appeared to be attached along the notch which is usually the seat of the bladder. We soon located the stones, but were surprised to find them in what proved to be the hepatic and common ducts. It was necessary to divide the mesentery of the duodenum to reach the stones. Two stones were removed from the common and six from the hepatic duct. Both ducts were largely dilated. The stones were about the size of filberts. After removing the calculi we made a very careful search for the missing gall-bladder but without success. We discovered a papule very near the site of the cystic duct. Careful probing through the open hepatic duct failed to locate any vestige of the cystic duct. Although the patient had been sick for many years, there had been no well-marked attack of gallstone colic. The evidence of cholecystitis, with the resulting adhesions, was not present, and we were not confronted by the results of inflammation, as is so often the case; but, as we have already stated, the anatomical defects were distinctly peculiar. It was necessary to open the ducts widely in order to extract the stones. The patient had a slow recovery, due

to loss of bile and poor nutrition. This was further complicated by a duodenal ulcer, which reached its climax on the twenty-eighth day, when a severe hemorrhage nearly proved fatal. The bile ceased discharging from the wound in twenty-four days; recovery progressed rapidly from this time, the patient having fully recovered, and being able to leave the city for home at the end of six weeks.

Absence of the gall-bladder is comparatively rare, but we find that a number of well-authenticated cases have been reported. Gay[1] has collected 19 cases, in 6 of which "absence" was the only abnormality. In 5 of these the patients were from twenty-five to sixty-five years of age. As may be supposed, the majority of cases are seen in young children and at the postmortem table. (See Eshner.) Nearly all of the important information upon the subject will be found in the articles by F. Fink[2] and A. Bubenhofer.[3] It is important that these cases should have careful inspection, and rigid search be made for apparently absent gall-bladders. Mistakes are made by men of more than average experience. It may be taken for granted that in the presence of severe inflammatory changes the gall-bladder is merely lost from view or mistaken for one of the ducts. I have on more than one occasion had to open the common and hepatic ducts before clearing up a case of doubtful diagnosis. The deeply planted gall-bladder, which has shrunk to the size of one of the ducts, is especially difficult to locate.

It is important that we should know that the absence of the gall-bladder is not necessarily a serious matter. Several of the lower animals do very well without such a viscus. The elephant appears large enough to need one, but does well without it. The deer, goat, and other animals are likewise not supplied with gall-bladders, yet we are not aware that they suffer from any of the results of gallstone or biliary disease. Finally, we note in the literature the uniform testimony regarding the dilatation of the bile-ducts in these cases. This may be due to obstruction alone, or it may be a compensatory dilatation of the hepatic duct, as may be seen after certain cases of cholecystectomy.

[1] Trans. Chicago Path. Soc., 1902, v, 108.

[2] Ein Fall von Vortauschung der Gallenblase, Prag. med. Woch., 1904, xxix, 245.

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REVIEWS.

DISEASES OF THE BREAST, WITH SPECIAL REFERENCE TO CANCER. By WILLIAM L. RODMAN, M.D., Professor of Surgery in the Medico-Chirurgical College of Philadelphia, and the Woman's Medical College of Pennsylvania. Pp. 385; 69 plates; 42 other illustrations. Philadelphia: P. Blakiston's Son & Co., 1908.

THIS is an interesting, accurate, and valuable addition to the literature of mammary surgery. Dr. Rodman's work shows thorough familiarity with the history of the various operative procedures, a full understanding of their most modern modifications, and extensive personal experience. If occasionally somewhat radical in his teachings—*e. g.*, in the advocacy of the removal of the pectoralis minor in all cases of carcinoma mammæ, and the exploration of the supraclavicular space in the majority of cases—it must be admitted that it is safer to err in this than in the reverse direction.

As a rule, the author's dicta represent the best recent surgical opinion, and may safely be followed. He is certainly correct when he says: "In suppuration the danger consists not in doing too much, but in doing too little. Early and free opening of the affected parts will invariably give satisfactory results, whereas delay, procrastination, and loathness to use the scalpel freely, when it is employed will be followed by extensive destruction of tissue."

His mention of the possible advantage of the "opsonic" treatment in tuberculosis of the breast is properly conservative. It is true that "there is no reason to doubt that it would do good in this form of the disease as well as in others," but it is also true that "it should not be used as a substitute for operation, which has been proved to be efficacious, but as a supplement to operation, with the view of hastening recovery by increasing the opsonic power of the blood."

The advice to practise plastic resection of the gland in cases of cyst, but to have an immediate examination—*i. e.*, while the patient is still anesthetized—of the affected tissue, and to proceed to full excision if carcinoma is present, is sound. Many breasts are uselessly sacrificed, on the one hand, and no small number of patients, on the other, from failure to appreciate and follow this excellent rule.

In the treatment of keloid, the use of the *x*-rays as preliminary to operation is wisely recommended, but no mention is made of the occasional benefit following the administration of thyroid extract in

such cases, or, at least, in cases of hypertrophied cicatrix, clinically indistinguishable from keloid.

In considering the etiology of carcinoma the author perhaps follows too implicitly the teachings of Orth, and correspondingly minimizes the strength of the arguments for classing cancer with the infectious diseases. He might also, in spite of the statistics of Williams, have safely been more positive as to the influence of trauma and chronic inflammation in favoring the development of cancer, especially in view of the fact that he himself mentions that "all forms of carcinoma are generally found at points subject to persistent irritation."

He is certainly right in condemning the preliminary use of x-ray treatment before operation, and most surgeons will agree that the "practice cannot be too pointedly condemned, inasmuch as it has been productive of little, if any, good, even in a minority of cases, and in all wastes valuable time—possibly allowing internal metastases to occur before operation is instituted." But in superficial recurrences, and in inoperable sarcomas, some benefit—occasionally great benefit—may be expected, and in rare cases of inoperable cancer there have been relief from pain and shrinkage of the tumor. This coincides with the experience of surgeons everywhere.

The illustrations are excellent, especially those explanatory of the operative methods, and the physical features of the book are very attractive. The author is to be congratulated on both the contents and the appearance of the book, which is sure to be well received by the profession. J. W. W.

MODERN CLINICAL MEDICINE. DISEASES OF THE NERVOUS SYSTEM. Edited by ARCHIBALD CHURCH, M.D. An authorized translation from *Die Deutsche Klinik*, under the General Editorial Supervision of JULIUS L. SALINGER, M.D. Pp. 1205. New York and London: D. Appleton & Co., 1907.

THIS is a rather imposing volume of 1200 pages. It suffers from the ordinary defects and advantages of a book written by many authors. Certain parts of the general subject of nervous diseases are omitted or treated too briefly, others too fully, and there is a moderate amount of repetition. On the other hand, certain phases of the subject, which should probably be omitted from a text-book, are treated with detail, and some of the articles are written by men thoroughly familiar with the subject from long years of more or less special devotion to it and form monographs of permanent value. The English translation is fairly good. The style varies less than in the German original, which is an advantage. The fact that some of the articles are written in a distinctly more conversational or lecture style than otherwise does not seem to render them in any respect

easier to read. There is an adequate number of illustrations, the majority of which are of value in elucidating the text. Many of them are diagrams or reproductions of tracings, but not a few are pictures of pathological specimens or of patients illustrating the symptomatology of disease or the application of different forms of mechanical treatment. The colored illustrations are perhaps on the whole the least successful, although many are excellent. Colors have also been used for the purpose of making some of the diagrams clearer. The brief, first section upon the macroscopic anatomy of the central nervous system, by Rothmann, is clear and considers the subject to a certain extent from a clinical standpoint. In the section on histology, Rosin, as was to be expected, introduces a good many descriptions of the staining methods. The article, however, is excellent, even if somewhat too scientific for a clinical text-book on nervous diseases, and it is admirably illustrated. He accepts the neuron theory unreservedly, and classifies the various diseases of the central nervous system according to the different neurons involved with a separate division for the inflammatory conditions. In the limits of a brief review it is not possible even to notice all of the individual articles. It may be noted, however, that the section on general neurological diagnosis, by Schuster, is rather unsatisfactory, the part on the significance of the reflexes being particularly inadequate. Modern aids in the diagnosis of diseases of the brain is a curious paper, that might have been extended with advantage, and includes a description of lumbar puncture, which, as treated separately by Quincke, is the most admirable article in the whole book, its value being enhanced by a very full bibliography. Wernicke writes on aphasia. The article is entirely according to the old school, and does not discuss the modern views of Marie. Gutzmann gives a very excellent account of the disturbances of speech, with some curious tables and diagrams. The article on tumors of the spinal cord is merely adequate; that upon myelitis and particularly the article on tabes dorsalis, by Erb, are masterpieces. The latter is written in the breezy controversial style peculiar to the author, and is most thorough in every department.

Among the other articles of distinct excellence are that upon heredity ataxia, by Lüthje; on the paralysis of the peripheral nerves, by Bernhardt, practically a condensation of his larger work; and upon neuritis and polyneuritis, by Kassirer. Edinger discusses headache, and Erb gives an excellent account of paralysis agitans. Franckl-Hochwart discusses athetosis, tetany, and myatonia congenita. Remak's article on localized spasm is interesting because it presents rather clearly the little that is definitely known about this condition. Eulenburg, in his article upon exophthalmic goitre, justly condemns sympathectomy in the treatment. His article on sexual neurasthenia is on a par with most of the articles upon psychopathia sexualis, exalting the subject and drawing

conclusions from insufficient data. Hysteria, by Ziehn, is very good, but the remaining articles on epilepsy, traumatic neurosis, occupation neurosis, and cerebral hemorrhage and embolism have been written hastily and are not worth the company they keep.

J. S.

OBSTETRICS. A TEXT-BOOK FOR THE USE OF STUDENTS AND PRACTITIONERS. By J. WHITRIDGE WILLIAMS, Professor of Obstetrics in the Johns Hopkins University; Obstetrician-in-Chief to the Johns Hopkins Hospital, Baltimore. Second edition; pp. 950; 682 illustrations. New York and London: D. Appleton & Co., 1908.

FROM our careful reading of the first edition of this work we were confident that the profession would afford it a gratifying reception. This prophecy has been justified by the appearance of the second edition at this early date. In our original review we gave it as our opinion that, as a scientific exposition of the subject in English, the work of Dr. Williams stands alone. We have no reason to be less emphatic after the study of the present volume. There are some views with which we are not in accord, and there are certain procedures, proved by ample experience to be valuable, which could have been included with advantage. Thus we think that the premature induction of labor, in the presence of moderate contractions of the pelvis, cannot in all fairness be dismissed by a negation. Furthermore, we can not look upon the method advised for the closure of the uterine wound after the Cesarean operation as the best possible, and finally we would suggest that a description of the Voorhees and Pomeroy bags be included, even if those of Champetier-de-Ribes and Barnes are considered preferable by the author. We simply mention these instances as explanatory of our previous sentence. On the other hand, it gives us pleasure to reiterate our enthusiastic opinion of the book as a whole and to call attention to the most marked changes and additions which this edition presents. These, as stated in the preface, consist chiefly in an entire rewriting of the chapters upon the development of the ovum and upon the toxemias of pregnancy, together with the addition of sections in which the metabolism of normal pregnancy, vaginal Cesarean section, pubiotomy, and contractions of the pelvic outlet have been considered. We would especially call attention to the chapter upon the toxemias of pregnancy, as it is the best exposition of this vexed ground which has as yet appeared.

That such an amount of revision and addition of new material has been found necessary in so short a period as has elapsed since the first edition, is a tribute to the advance of the science of obstetrics and to the well-known progressive spirit of the author. W. R. N.

THE PREVENTION OF INFECTIOUS DISEASE. Being the Lane Lectures, delivered at Cooper Medical College, San Francisco, in August, 1906, and revised for publication. By JOHN C. MCVAIL, M.D., D.P.H. (Cambr.), F.R.S.E., County Medical Officer for Stirlingshire and Dunbartonshire, Ex-president of the Incorporated Society of Medical Officers of Health of Great Britain, and of the Incorporated Sanitary Association of Scotland. London. MacMillan & Co., 1907.

IN this country the question of public health organization and sanitation is receiving today well merited attention, and though, undoubtedly, great improvements have come about in the last few years through this interest aided by hard work, still there remain any number of important problems to be settled. As this is particularly true of the smaller towns and country districts, it is with great interest that one reads in this series of Lane Lectures the measures which have been adopted to prevent the spread of infectious and contagious diseases in Scotland and England. In this book Dr. McVail gives the reader a very good description of the way in which the Health Board of Great Britain has dealt with such diseases as typhus, typhoid, plague, measles, diphtheria, and scarlet fever. Though a portion of each chapter is devoted to a rather elementary discussion of the cause and prophylaxis of the disease under discussion, the greater portion of the lectures is concerned with accounts of the work of the Health Commissioners in combating the spread of the disease. It is interesting to note that in England and Scotland cases of typhoid fever are required to be taken to "fever hospitals," or isolated at home. Though the various methods by which the disease is spread are discussed in some detail, no mention is made of "bacillus carriers," a source of infection which seems to be of the greatest importance. It is stimulating to learn that active measures are being instituted against the spread of measles, a disease which McVail states has a mortality of 10 to 20 per cent. in children under three years of age. After the age of five the mortality is but 1 per cent., so that the policy which has been adopted is to try to delay the attack, which is practically inevitable, until after the sixth or seventh year. This has been accomplished, to a certain extent, through inspection of schools, through which institutions the disease is principally spread. In the chapter upon scarlet fever there is a good discussion upon the question of hospital ventilation, and though some of the methods of natural ventilation in vogue in Great Britain are not applicable to our American climate, still an estimate of their use is instructive. The book does not purport to be, and is not, a systematic treatise upon hygiene, but as a series of lectures, illustrating the methods adopted by a Board of Health for the prevention of certain specific diseases, it is interesting and instructive. W. T. L.

A Manual of Venereal Diseases, by Officers of the Royal Army Medical Corps. Introduction by Sir Alfred Keogh, K.C.B., Director-General of the Army Medical Service; History, Statistics, Invaliding, etc., by Lieut. Colonel C. N. Melville, R.A.M.C., Secretary to the Advisory Board; Clinical Pathology and Bacteriology, by Colonel Leishman, R.A.M.C.; Clinical Course and Treatment, by Major C. E. Pollock, R.A.M.C. Pp. 282. London: Henry Frowde, Oxford University Press; Hodder & Stoughton, 1907.

This manual is the outcome of the report made, in 1905, to the British Army Medical Advisory Board, by a committee appointed to consider the question of the treatment of venereal disease in the army. The subjects discussed are syphilis, gonorrhœa, and soft chancre.

Prevention of these diseases receives merited consideration; and when it is recollected that more than 9 per cent. of the army is incapacited on this score, the question of prophylaxis is seen to have great economic importance entirely apart from any question of morals. Colonel Melville, after briefly outlining the history of the methods of prevention attempted in military surgery, comes to the conclusion that besides mere discipline and punishment, the high ideal of abstinence from illicit intercourse must be constantly held before the soldier. He would be inclined "to allow a man to have two primary attacks of venereal disease without making more than a Company Entry. The third primary attack should be made a Regimental Entry." He says: "The making up of lost duties is a practical idea. The hardened sinner would know quite well that the longer he stayed out of hospital concealing his disease, the longer he would probably have to remain in hospital for recovery, and the more guards, etc., he would have to make up." In urging the ideal of continence, he asserts that "all other systems of prevention accept incontinence as a necessary part of male life, and aim at making it safe. They place the ideal, if it can in any way be called an ideal, as low as possible, and figures prove that they fail in any way, to attain their ideal, that is absolute safety."

The pathology, diagnosis, and treatment of the venereal diseases, and their commonest complications, are comprehensively detailed; the soft chancre being defined as "a contagious ulcer of the genitals, caused by the inoculation of the bacillus of Ducrey;" and the volume closes with tables and appendices showing the percentage incidence of venereal diseases in the army, and giving formulæ and outlines for the administration of mercurials in syphilis, and the solutions for injection and irrigation in gonorrhœa. A. P. C. A.

THE OPERATIONS OF GENERAL PRACTICE. By EDRED M. CORNER, M.A., M.C., M.B. (Cantab.), B.Sc. (London), F.R.C.S. (England), Surgeon in Charge of Out-Patients at St. Thomas' Hospital, London; and H. IRVING PINCHES, M.A., M.B., B.C. (Cantab.), M.R.C.S., L.R.C.P. (London), Clinical Assistant to the Children's Hospital, Great Ormond Street, London. Pp. 296; 170 illustrations. London: Henry Frowde, Oxford University Press; Hodder & Stoughton, 1907.

THE authors state that in this work they have attempted to meet a deficiency in professional education. This is, of course, a laudable ambition, but when it leads to the attempt to render general practitioners, with no training or previous experience in surgery, capable of undertaking such operations as those for the radical cure of hernia, for tuberculous cervical adenitis, for suprapubic cystotomy, plastic resection of mammary tumors, necrosis of the femur, complete rupture of the perineum, etc., etc., we think that the authors have rather overshot their mark. They expatiate at some length upon the fact that the old-time division of operations into major and minor has been largely obviated by aseptic technique; but they appear to forget that aseptic technique is acquired not from the perusal of text-books, but from prolonged apprenticeship in the operating room. Many of the "operations" described, such as the opening of a boil, gastric and vesical lavage, tapping a hydrocele, vaccination, etc., are properly enough done by the family physician; and while all the operations included are, indeed, those of general surgery, this term should not, we submit, be used as synonymous with operations which do not require surgical skill for their performance. The authors have avoided writing, on the one hand, a "Minor Surgery," and on the other, an "Operative Surgery." The result is an unhappy hybrid, which is "neither fish, flesh, fowl, nor good red herring."

With this warning, the volume may be commended as presenting adequate descriptions of the usual run of operations, sufficiently illustrated by diagrams and by cuts of apparatus. A. P. C. A.

A LABORATORY HANDBOOK OF BACTERIOLOGY. By RUDOLPH ABEL, of Berlin. Translated from the tenth German edition, by M. H. GORDON, M.A., M.D. (Oxon.), B.Sc. Pp. 224. London: Henry Frowde, Oxford University Press, 1907.

THIS little handbook should prove a valuable and acceptable addition to the libraries of laboratory workers not alone of the medical, but of allied professions. It is adapted not only to workers new to laboratory methods, by giving them proper ideas regarding

general bacteriological technique, and by enabling them, quickly, to establish a workable laboratory routine, but also to the experienced bacteriologist, by presenting briefly the many little details of media preparation, staining methods, etc., so likely to be forgotten. Its chief merit lies in its compactness.

The first eighty pages take up the care of the microscope, the principles of sterilization and disinfection, the preparation of media, and a general discussion of cultural and staining methods. The next eighty pages are devoted to individual bacteria, considering chiefly the commoner and more important ones, in relation to special media to be used, cultural reactions, and best staining methods. Deserving of especial mention are the twenty-odd pages devoted to the typhoid bacillus. The last sixty pages give the methods for obtaining material from the body for bacteriological examination; of inoculation, postmortem examination, etc., of animals; of bacteriological examination of water, shellfish, etc., and of dust and air.

For the last third of the book, due credit must be accorded to Drs. T. J. Horder and A. C. Houston for their careful revisions and amplifications, and especially to Dr. Gordon—the translator—for his chapter on Immunity, which consists of a series of abstracts of articles by Wright, Douglas, Leishman, and others regarding technique and methods.

To the general practitioner, desirous of establishing a little working laboratory of his own, this handbook will assuredly be welcome. As stated in the author's preface, his manual is not intended to supersede or replace the larger text-books on the subject, but to serve as a supplement to them and as a guide to practical laboratory work, and as such it amply fulfils its author's purpose. V. L.

THE OPERATING ROOM AND THE PATIENT. By RUSSELL S. FOWLER, M.D., Professor of Surgery in the Brooklyn Post-graduate Medical School, New York. Second edition; pp. 284; 33 illustrations. Philadelphia and London: W. B. Saunders Co., 1907.

IMMEDIATELY upon its publication, Fowler's *Operating Room and the Patient* established for itself a useful place in the armamentarium of the surgeon, especially surgical internes of hospitals, and the nurse. The new edition contains all the good features of the old, and several additions. The chapters of general considerations in the after-treatment and on the instrument and supply room have been much amplified, and new chapters dealing with wound complications and their treatment have been added. The book unquestionably is of much service to all that have to do in any way with operative technique; to surgical internes and nurses it seems as though it were almost a *sine qua non*. A. K.

PROGRESS

OF

MEDICAL SCIENCE.

MEDICINE.

UNDER THE CHARGE OF

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The Diagnosis of Ulcer of the Stomach.—BÖNNIGER (*Berl. klin. Woch.*, 1908, xiv, 396) asserts that the pain of gastric ulcer may be so characteristic as to justify the diagnosis of the condition. It is a matter of common experience, however, that the pains are often atypical or that they may closely resemble the pains of other diseases. To aid in the recognition of the pains arising from the presence of an ulcer in the stomach, Bönniger makes use of a dilute solution of hydrochloric acid which he pours into the empty stomach through the stomach tube. The proceedure is as follows: The stomach tube is introduced into the fasting stomach early in the morning. If one obtains no fluid, 100 c.c. of water is poured in, and after shaking movements on the part of the patient it is withdrawn and examined for acids, blood, albumin content, epithelial cells, and mucus. (This examination Bönniger finds very helpful in all stomach cases.) In ulcer no pain is caused by the introduction of the water, and it serves to eliminate psychic elements in the subsequent use of the acid solution. Next, one introduces through the tube 100 to 200 c.c. of $\frac{N}{10}$ HCl into the stomach. In patients with ulcer of the stomach severe pain ensues at once—usually relieved by giving milk. In no other gastric disease, including carcinoma, has Bönniger obtained a like result. If no pain is produced by giving the $\frac{1}{10}$ normal acid, change of position and shaking are resorted to, so that the acid may be brought into contact with all parts of the gastric mucosa. Failure to elicit pain now means that the pains of which the patient complains do not result from the presence of peptic ulcer, according to Bönniger's experience. Two essentials for the successful carrying out of the test are an empty stomach and the absence of supersecretion with high acidity. The test is of doubtful value in cases of

ulcer when no pain exists; when the pain is atypical, it is a great aid. The test is further very useful in determining the efficacy of treatment; with improvement the pain produced becomes less, and entirely disappears when the ulcer is healed.

Gastric Secretion in Rectal Feeding.—MICHAEL (*Berl. klin. Woch.*, 1907, xliv, 1446) concludes, from examinations made by him in Ewald's clinic, that neither in healthy individuals nor in invalids does the administration of a nutrient enema lead to the secretion of gastric juice, at least for one-half to one hour after giving the enema. Rectal feeding is therefore not in any way harmful in gastric ulcer.

The Basophilic Granules in the Red Blood Cells in Anemias.—ASKANAZY (*Ztschr. f. klin. Med.*, 1907, lxiv, 288) has changed his views about the origin of these granulations. He formerly believed, with the majority of recent writers upon this subject, that the basophilic granules are derived from the breaking up of the nucleus of the red blood cell. His opinion now is that they are the result of changes induced by the plasma upon polychromatophilic red cells. He has observed that the more intense the polychromatophilic staining of the red cell is, the more numerous, the smaller, and the more closely placed are the granules; conversely, the coarser and more distinct the granules, the more the color of the protoplasm approaches the orthochromatic. The same things he finds true of the erythroblasts. Askanazy does not look upon basophilic granules as the normal physiological expression of the disappearance of polychromatophilia, for cells showing these granules are not present in the blood of the embryo, the newborn, or in the bone marrow. The granules appear only when, in abnormal conditions, the chemical or physical characters of the plasma are changed from the normal. The basophilic granules are of diagnostic importance only in lead poisoning. Askanazy agrees, then, with Grawitz and others that the basophilic granules found at times in the red blood cells are not nuclear in origin, but, unlike Grawitz and his followers, he considers them a sign of regeneration of the blood, not a sign of degeneration.

The Ophthalmic and Cutaneous Tuberculin Reactions and Other Methods for the Diagnosis of Tuberculosis.—WOLFF-EISSNER (*Beit. z. Klin. der Tuber.*, 1908, ix, 1 to 189) has presented a very comprehensive study of the diagnosis of tuberculosis. The methods for the positive diagnosis of tuberculosis are given as (1) the demonstration of tubercle bacilli; (2) the agglutination test (Arloing); (3) the tuberculin test (Koch). The latest modifications in the use of tuberculin, namely, the cutaneous reaction (v. Pirques) and the conjunctival reaction (Wolff-Eissner, Calmette), are considered at length. After giving in detail the technique of administration, the author sets forth his results with these new diagnostic procedures. He finds that the conjunctival reaction is very much more marked in early cases (patients with few physical signs or none at all), while in the third stage of pulmonary tuberculosis the reaction may fail. Others have found failure of reaction in cases which advanced rapidly, and they have therefore criticised it, but this Wollff-Eissner considers one of its most valuable features; for in all such cases that he has observed the diagnosis was readily made by other means, and

the absence of the reaction is, then a very valuable prognostic sign. Lack of reaction in manifest cases of tuberculosis means, he thinks, diminished powers of resistance on the part of the body, "an ominous sign." Cases are cited to substantiate this point.

Wolff-Eissner thinks it is too early to speak with confidence of the value of the cutaneous and conjunctival reactions in suspected cases of tuberculosis, as it is scarcely six months since the methods were introduced, and sufficient time has not elapsed to observe the further course of such cases. His experience, so far as it goes, is that the conjunctival reaction corresponds in results practically with subcutaneous injection of tuberculin. As to repetition of the conjunctival test, Wolff-Eissner believes that a positive result following one or more negative tests indicates a latent process.

Among 192 patients in whom no evidence of tuberculosis could be found on careful physical examination, 96 gave a positive cutaneous reaction, 35 a positive conjunctival reaction. The author believes, from clinical and pathological studies, that patients having healed "latent" tuberculous foci react to the cutaneous test, while it is only the active processes which are revealed by the conjunctival reaction —and these only when the resisting powers of the body are sufficiently high. In this way the enormous difference in the number of positive reactions in patients supposedly non-tuberculous is explained.

The use of the conjunctival and cutaneous tests is considered in pediatrics, dermatology, ophthalmology, gynecology, psychiatry, and veterinary medicine. Theoretical considerations follow. In the sputum of the tuberculous Wolff-Eissner calls attention to the importance of lymphocytes. In early cases he finds that they may constitute 33 to 90 per cent. of all cells in the sputum. The lymphocytes may be increased before tubercle bacilli appear in the sputum and even later with a mixed infection. The similar increase in the relative number of lymphocytes in the sputum in pertussis can scarcely lead to confusion.

(The article is so full and contains such a wealth of material that it is not suitable for a short abstract.)

Animal Inoculation in the Diagnosis of Tuberculosis.—WEBER (*Münch. med. Woch.*, 1908, lv, 321) calls attention to the great value of animal inoculation and its comparative neglect in the diagnosis of tuberculosis. Guinea-pigs are used because of their great susceptibility to the tubercle bacillus. The procedure is as follows: Pleural exudate or urine is centrifugalized and the sediment is transferred to a small quantity of sterile physiological salt solution; with the sputum about 0.5 c.c. of it is placed in the normal salt. The salt solution containing the suspected material is then injected into the lower part of the abdominal wall. An acute inflammatory process may result from the presence of organisms other than the tubercle bacillus; if this accident is avoided, however, an enlargement of the regional lymph glands up to the size of a lentil may be palpated within ten to sixteen days—rarely later, provided the animal has been infected with tubercle bacilli. The lymph gland is removed aseptically under ether, embedded in paraffin, and sections are stained for Bacillus tuberculosis. If bacilli are few in number, it may be necessary to inoculate several animals before a safe conclusion may be reached. Traumatism (pinching) in the region of

the lymph glands, as recommended recently by Bloch, may lead to an earlier swelling, but secondary infection with pyogenic cocci is common and greatly complicates the histological examination of the lymph gland. Weber emphasizes the futility of attempting to differentiate smegma and tubercle bacilli by staining methods alone, and strongly urges the more widespread use of animal inoculation in the diagnosis of tuberculosis. The time required is not great and the results obtained, with careful technique, are conclusive.

The Serum Treatment of Epidemic Cerebrospinal Meningitis.—Simon Flexner and J. W. Jobling (*Jour. Exp. Med.*, 1908, x, 141) note that in part of the work of the Commission appointed by the Department of Health of the City of New York an attempt was made to modify favorably the course of experimental injections with Diplococcus intracellularis (Weichselbaum) with sera prepared in several kinds of small animals. This was found to be successful in those experimented upon, and was tried on human subjects, but the cases were so few that the results were not included in the first report. Since then the diplococcus antiserum prepared by Flexner and Jobling from the horse has been successfully tested in cases widespread over this country and abroad, and this article is the report of the results obtained with the serum. These results are those in 47 cases reported upon, excluding 4 fatal cases which were not favorable for a reliable test. There were 79.9 per cent. of recoveries and 20.1 per cent. of deaths. Although the number of cases was small, yet the treatment was begun at such various times in the course of the disease that the tests were particularly severe. The results, therefore, have more value. When given within the first three days of the sickness the recoveries in 18 cases were 88.9 per cent. This is very encouraging when the usual high mortality is considered with other forms of treatment. In 25 instances the termination of the disease after injection could be followed; in 13 the termination was by lysis; in 12 by crisis. In a number of other cases the termination of the disease, after an acute and violent onset, within forty-eight hours of the injection of the antiserum was striking and impressive. Once or twice, after an abrupt onset of the symptoms lasting several days, relapses occurred, which were as promptly controlled by another injection of the serum as was the original injection. The introduction of the antiserum into the body by means of the spinal canal was justified (1) by the advantage of bringing the antiserum into direct contact with the focus of infection and inflammation, and (2) by the knowledge that elimination of colloids and crystalloids even from the blood stream into the cerebrospinal fluid is a slow and imperfect process in health, and probably more so in inflamed states of the membrane. In this report all of the cases received intraspinal injection. The effect noted by the direct application of the antiserum on the diplococci present in the exudate of the cerebrospinal membrane is most striking, and indicates rapid degeneration and arrest of the free multiplication of the cocci. Flexner and Jobling think that the dangers of anaphylaxis can be neglected at present. The early injection (within the first three days) gives the most promising results, and yet favorable effects have been recorded in many cases even as late as the eighth week. At present the dose of the serum rests upon an empirical basis,

but the effects of the larger doses used lately can only be noted in many more reported cases. Flexner and Jobling are firm in their belief that more cases must be reported before any final conclusive proofs of the beneficial effects of the antiserum can be stated. Yet, certainly, from the beneficial effects so far noted, it deserves widespread tests; these should be carefully controlled, in order to prove or disprove the value of the antiserum. Since this article was prepared for publication a number of cases have been reported with successful results following the injections of the antiserum.

The Hemolytic Action of Ankylostoma Duodenale.—PRETI (*Münch. med. Woch.*, 1908, lv, 436) has collected the parasites from the stools of patients after administering to them extractum filicis maris or thymol. The worms were then washed in physiological salt solution several times and finally rubbed up in a mortar with a small quantity of the salt solution. The turbid suspension obtained in this way was neutral in reaction. Increasing quantities of the suspension were added to a 5 per cent. suspension of washed red blood corpuscles, placed in the incubator at 37° for two hours, and then in the ice chest until the following morning. Preti finds that Ankylostomum duodenale contains a hemolytic substance which is active not only upon the red blood cells of man, but also upon those of the dog, rabbit, ox, and guinea-pig. The hemolytic agent is insoluble in the normal salt solution, slightly soluble in alcohol and ether; it is thermostabile. Addition of lecithin increases its activity, and cholesterin does not neutralize it. After the suspension of the parasite has been digested by trypsin, the hemolysin is soluble in water. It was found that 2.5 mg. of moist ankylostomum sufficed to hemolyze 1 c.c. of the corpuscle suspension. The hemolysin discovered belongs to the lipoids and is analogous to those found in organ extracts, in bothriocephalus, and in sclerostoma. The relation of this hemolyzing body to the anemia produced by ankylostomum duodenale, the author will discuss in another paper.

The Parathyroid Glands in Osteomalacia.—ERDHEIM (*Zentralb. f. d. med. Wissensch.*, 1908, xlvi, 163) determined by animal experiments that a relationship exists between the parathyroid glands and calcium metabolism. Extirpation of these glands in rats led to fractures of the teeth and defective production of dentine. On the basis of these experiments, Erdheim examined the parathyroid glands of man in 6 cases of osteomalacia and compared them with the glands of 9 other patients dying of other diseases. The result was: Case I: An enormous hyperplasia of one of the parathyroid glands; in the remaining three glands, no change. Case II: One gland enlarged; all showed colonies of newly formed tissue. Case III: All four parathyroid glands, of which three were enlarged, showed signs of atrophy. Cases IV and V: No enlargements of the glands, but changes similar to those in Case II. Case VI: No changes. Tetany is often seen in patients suffering with osteomalacia. Tetany is definitely the result of injury to, or removal of, the parathyroid glands. Possibly a similar relationship exists in osteomalacia combined with tetany.

SURGERY.

UNDER THE CHARGE OF

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The Practical Application of Local Anesthesia to Fractures.—LERDA (*Zentralbl. f. Chir.*, 1907, xxxiv, 1417) says that general anesthesia is not always desirable for the reduction of fractures and the application of the necessary retentive dressing. The movements of the patient during the stage of excitement may be so violent as to require the aid of several assistants, and often the patient's stomach is full, so that the giving of a general anesthetic may prove dangerous. Local anesthesia has been employed with satisfactory results by several writers, and Lerda has used it during the last two years in 30 cases of fracture with unqualified success. The most important point in the technique is to locate exactly the line of fracture, in order that it may be well anesthetized. A syringe with a long, strong needle is best. The anesthetizing fluid should be injected first between the two fragments, then around the fracture region, so that the medulla, periosteum, and surrounding tissue will be well infiltrated. Lerda has almost always employed a cocaine solution (1 part of cocaine to 200 of physiological salt solution), to which is added some adrenalin (1 drop of a 1 to 1000 solution to 1 c.c. of the cocaine solution). A few minutes after the injection, light active and passive movements of the broken limb are painless. After six to ten minutes the anesthesia is complete, muscular contraction is absent, and the manipulations for the reduction can be carried out. The patient will complain only of an unpleasant feeling of tension due to the swelling of the tissues from œdema and hemorrhage. Lerda had the opportunity, in the same patient and for the same fracture, that of the lower end of the radius, to compare the relative merits of reduction without and with local anesthesia. The latter proved to be a decided advantage. Most of the cases in which the method was employed were fractures of the lower end of the radius. Good results were obtained in fractures of one or both bones of the forearm and of the humerus. Fractures of the elbow, except supracondyloid fractures of the humerus and fractures of the olecranon, are not suitable for this method, because they usually cannot be localized exactly enough to permit a rational anesthesia. For the same reason, fractures of the femur will probably be unsuitable, also because of their depth. Probably in a few cases of supracondyloid fracture of the femur it would be successful. It is especially applicable to fractures of the leg, the clavicle, and the ribs.

Coxa Valga and its Varieties.—Mauclaire and Olivier (*Archiv. gén. d. chir.*, 1908, ii, 1) define coxa valga as an affection of the hip, characterized by a valgus position of the whole lower extremity and an abnormal direction of the femoral neck (hyperflexion, hypoflexion, anteversion, retroversion). It has been found with the following deformities of the femoral neck: simple hypoflexion, hypoflexion with abnormal anteversion or with simple retroversion, hyperflexion, hyperflexion with abnormal anteversion or retroversion. The clinical varieties are: (1) Those occurring at birth, (*a*) by the essential deviation of birth, (*b*) in congenital luxation, on the luxated bone or on the opposite one by compensation, and (*c*) in hydrocephalus. (2) After birth it has been observed in osteomyelitis, achondroplasia, rachitis, exostoses, tuberculosis, fractures, epiphyseal separations, scoliosis, dislocations of the hip, ankylosis of the knee, club feet, paralysis, amputations, prolonged confinement to bed. Pathologically, there are four mechanisms: (*a*) Congenital coxa valga from a defect in development of the position of the femoral head; (*b*) coxa valga acquired by osteitis, traumatism, or by station (compensatory). The physical and functional symptoms vary according to the variety. The one chief symptom is abduction and external rotation of the lower extremity. The skiagraph permits an exact diagnosis of the different varieties. An abnormal direction of the neck of the femur is necessary. As for the treatment, if the coxa valga is essential and original, reduction with immobilization in one or more successive plaster dressings is necessary. Myomotomy and osteotomy may be indicated. If the coxa valga is symptomatic, it is evidently necessary to treat the causal condition.

Operations for Suppuration and Gangrene of the Lung.—Körte (*Arch. f. klin. Chir.*, 1908, lxxxv, 1) says that acute suppurative processes of the lung, without putrid decomposition and without sphacelus formation, should be treated for a few weeks by internal therapy. If, then, there is no abatement of the suppuration and the fever continues, pneumotomy should be done at once. In such cases this gives a good prognosis. Acute gangrene of the lung is to be treated as soon as possible by free exposure and excision. Only those bronchiectatic cavities confined to one lung should be operated on. The operation should be radical, with extensive resection of the thorax, free incisions, and, if healing does not result, the resection of a lobe of the lung.

McBurney's Point.—Lanz (*Zentralbl. f. Chir.*, 1908, xxxv, 185) concluded, after observing in a statue the furrow passing between the two anterior superior spines of the ilium, to make his incision for laparotomy in the lateral portion of the abdomen, as for appendicitis, in the line of this furrow, whenever a cosmetic effect was important. The deeper part of the incision was carried out on the McBurney principle of following the fibers of the different muscle layers. He found that by this incision he came more directly on the appendix than by the usual oblique incision. This led him to investigate carefully upon 20 patients the exact location of the appendix. He found that the attachment of the appendix to the cecum is more constant than is generally supposed, and that McBurney's point has nothing to do with the situation of the appendix. Much more frequently McBurney's point corresponds to

the medial side of the ascending colon, and generally to a point 4 to 5 cm. above the base of the appendix. More rarely it lies over the angle formed by the ileum and ascending colon, and only in pathological cases, as in large abscesses, is it in the region of the base of the appendix. As a rule, the base of the appendix lies at the junction of the middle and right third of the interspinal line, *i. e.*, about a finger's length from the right anterior spine. If McBurney's point corresponded to the base of the appendix, it would not explain the significance of the tenderness at this point, since it is the point of the appendix which is most frequently diseased. Usually the corresponding sympathetic ganglion is made responsible for the pain. It has also been ascribed to a swollen lymph gland and to lymphangitis. Of 119 appendectomies, it was observed that in a few months after operation the tenderness at McBurney's point had disappeared in 93 cases, and that in 26 it still remained. The diagnostic value of tenderness at McBurney's point is therefore not always positive. Palpation may increase the inflammatory process in an inflamed appendix or set up inflammation in a normal one.

The Transfusion of Blood from the Vena Cava to the Portal Vein by Means of a Termino-lateral Anastomosis.—MEYER (*Zentralbl. f. Chir.*, 1908, xxxv, 217) calls attention to the work of Tansini, who performed the operation on dogs for the making of an Eck fistula between the portal vein and the cava. This operation has been done in man by Vidal. Meyer takes up the question of breaking the continuity and occasionally resecting a portion of the cava proximal to the entrance of the renal veins. Up to the present time this has been considered possible only when a previously existing stenosis of the cava had prepared it for ligation by improving the collateral circulation. Meyer offers a method by which the cava may be immediately ligated and divided and its blood allowed to escape at once into the portal vein. A dog was placed on a roll-shaped cushion for the laparotomy and an oblique incision made, beginning about 2 cm. below the xyphoid process and extending 10 cm. in the direction of the right anterior superior spine of the ileum. After opening the abdominal cavity the intestines and pancreas were drawn out of the wound, wrapped in a towel wrung out of a warm normal salt solution and placed on the left side. The portal vein was then freed as far as possible from its bed of transparent connective tissue with grooved director and forceps. About 1.5 cm. of its length was then included between rubber clamps, the jaws of which were covered with rubber tubing. The cava was then liberated from its bed in a similar manner and ligated on the proximal side, while on its distal side it was clamped with similar forceps. It was then divided transversely close to the ligature. The open end of the cava was then anastomosed by sutures to a longitudinal opening made in the corresponding side of the clamped off portion of the portal vein. The extreme tenderness of the latter made a very fine suture and gentle manipulations necessary, lest the coats tear and bleeding occur from the stitch holes. Nine days after the operation the dog was shown before the Berlin Medical Society. Sugar or albumin appear in the urine either immediately after the operation or later. The dog lived fifteen days, and thus proved that he could tolerate the transference of the caval blood through the liver, while other dogs with insignificant stenosis of the portal vein died in two days following the operation, with symptoms of hemostasis.

Concerning Diffuse Hyperostosis of the Cranial and Facial Bones. Osteitis Deformans Fibrosa (Virchow's Leontiasis Ossea).—BOCKENHEIMER (*Archiv f. klin. Chir.*, 1908, lxxxv, 511) considers that the name, leontiasis ossea, is not suited to this disease. It is best designated by the term diffuse hyperostoses of the cranial and facial bones. The pathological process appears to be identical with osteitis deformans (Paget). The early diagnosis and differential diagnosis are best accomplished by the *x*-rays. The etiology is due to a faulty metabolism, so that it is in this respect probably related to other diffuse hyperostoses of the bones, as in gigantism and acromegaly.

The Treatment of Racemose Arterial Angioma.—CLAIRMONT (*Archiv f. klin. Chir.*, 1908, lxxxv, 549) says that for the extirpation of such a growth the preliminary ligation of the afferent vessels, as is now carried out, is not absolutely necessary even when the growth is extensive. He reports a case of a man, aged forty-three years, with a racemose arterial angioma covering the greater part of the scalp. It was especially prominent on the left side in the temporal, parietal, and occipital regions, and in the same regions on the right side, but to a less extent. The left temporal artery in front of the ear was dilated to about the thickness of three fingers, and this dilatation extended below as far as the angle of the jaw. Over almost the whole of the involved area of the scalp the tumor was well developed, but only a few small dilated vessels affected the frontal region. The skiagraph taken in the frontal plane showed that the grooves for the middle meningeal artery were broadened and tortuous. Operation was performed with the patient in the sitting position and under morphine-chloroform anesthesia. An incision was made through the skin and subcutaneous tissue over the whole skull from left to right, beginning a finger's breadth above the outer canthus of the left eye. No preliminary ligatures were employed. The incision was first directed upward, and then was curved backward, crossing the middle line at the anterior part of the vertex of the skull, ending on the right side on a level with the external auditory canal at about the posterior border of the mastoid process. The incision was made step by step under compression of the large vessels against the scalp. The posterior branch of the temporal artery, about the thickness of the thumb, was isolated under the anterior lip of the incision and was divided between ligatures. The tumor was confined almost entirely to the scalp posterior to the incision. This portion of the scalp was separated from the skull like a flap and turned backward. This part of the operation was very bloody. The vessels entering the tumor from three sides were sought and controlled by numerous ligatures. This was particularly troublesome toward the right cheek and in the region of the right occipital artery on account of the rich anastomosis. The operation had lasted about one and one-half hours by this time, and it seemed that as much more time would be required to complete it. The pulse had become weak, and it was decided to postpone the extirpation of the tumor to a second operation as Krause had done. The skin flap was replaced, wrapped in sterile gauze, and an aseptic bandage applied. After the head was lowered and salt solution introduced intravenously the patient reacted quickly. Three days after the first operation the extirpation was completed under morphine-chloroform anesthesia. The flap was turned outward again

and the loosened edges of the tumor easily found. The limits of the tumor were more definite because the vessels had thrombosed and the connective tissue between it and the skin had become thicker and looser from the œdema. The separation of the tumor, although difficult and time consuming, was successful throughout except for occasional perforations of the thin skin. The skin incision, now considerably larger than the wound defect, was trimmed accordingly and sutured to the anterior edge of the original incision. As was expected, a portion of the skin flap necrosed. This was about the area of the size of the palm, and was later covered by skin grafts by the Thiersch method. Here and there secretion collected under the flap and was evacuated, partly through the perforations made at the time of the operation and partly through new punctures. The remaining dilated portions of the right temporal and frontal arteries later diminished in size. On the day before he was to be discharged, however, he suddenly became unconscious without convulsions. After fifteen minutes he recovered sufficiently to speak intelligently and to permit a taking of the nerve findings. This proved to be normal except for a slight paresis of the right side of the mouth, due to a slight wound of the cheek, which had required two stitches. The history showed no evidence of previously occurring epileptic attacks.

Extracapsular Radical Resection of Tuberculous Elbow Joints.—LOSSEN (*Deut. Ztschr. f. Chir.*, 1908, xcii, 120) says that for the last thirteen years, in Bardenheurer's clinic, all tuberculous joints which have not shown a tendency to heal after a short conservative treatment have been operated on by Bardenheurer's method of extracapsular radical resection. The tuberculous area should be extirpated in sound tissue whenever possible without sparing joint ligaments, muscles, or their insertions, so that there shall be no remains of funguous tissue. If possible, none of the joint contents should be permitted to escape and soil the fresh wound surface. The indications for the operation have already been outlined by O. Wolf. In fresh cases an attempt should first be made to obtain a cure by the conservative method of immobilization in a plaster cast, giving at the same time iodoform injections. If improvement does not occur soon or the condition becomes aggravated, with increase of the swelling, pain, and abscess formation, resection should be done. If when first seen sinuses have developed, Bardenheurer proceeds at once to resection, whether the patient is a child or an adult. After removal of all diseased tissue, firm primary union of ends of the bones is sought, in order to prevent the development of a flail joint. For this purpose cuneiform osteoplasty is employed by making a V-shaped notch in the lower end of the humerus, fitting the end of the ulna into the notch, and fixing the two bones together by a nail, which is allowed to emerge from the skin. In order to retain the power of pronation and to remove thoroughly all the tuberculous process, which by preference settles in the space between the upper ends of the radius and ulna, the radius is sawed off 2 to 3 cm. lower than the ulna and is covered over with muscle tissue. The radius cannot then adhere either to the humerus or the ulna. The skin and muscles are then sutured and the joint is fixed with a plaster cast.

THERAPEUTICS.

UNDER THE CHARGE OF

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The Treatment of Angina Pectoris.—ALLBUTT (*Folia Therapeutica*, 1908, ii, 3) considers that in angina pectoris we have to regard three purposes: (1) To mitigate, if possible, the lesion of the aorta; (2) to reduce the stresses; (3) to block the inhibitory influence on the heart. To combat the local affection we may use antidotes, as in acute rheumatism, for instance, salicylates, or the iodides. In syphilis the latter, with or without mercury, would be required. In aortitis from such causes as influenza we have to trust to nature, but in intermediate instances, as gout, we have tolerably effectual, although empirical, methods. In relieving tension we have first the use of gentle and frequent mercurials and salines in such patients as tolerate them. Then comes the promotion of normal metabolism, first by means of exercise, which must be regulated with care. The same is true of diet; no full meal should be eaten under mental or physical fatigue and all meals should be restricted in quantity, but, on the other hand, in nstances of defective appetite, stomachics, strychnine, pepsin, hydrochloric acid, etc., may be indicated. Alcohol, strong tea, and coffee must be forbidden. The angina itself should first of all be treated by confinement to bed, but in old patients we must carefully guard against pulmonary congestion in ordering recumbency. With regard to arterial dilators, particularly glyceryl nitrate, we have a drug which must be watched, for, while Osler states that, if necessary, he is not afraid to prescribe the 1 per cent. solution in doses of 30 minims thrice daily, Allbutt has noticed a tendency to habit formation, and considers that "the physician should hold the prescription in his own hands." With regard to the iodides, unless syphilis is present, 3 to 5 grains thrice daily are sufficient. Venesection may be employed if hyperpiesis is primary and persistent. Baths, massage, and electricity, if employed at all, must be used under the strictest surveillance. In the palliation of attacks the nitrites are our chief reliance, but Allbutt urges the importance of blocking the reflex by which the heart is inhibited. This seems to be best accomplished by means of atropine, and he is accustomed to advise its administration until the liability to an attack seems to have vanished, and on the access of an attack he orders an immediate hypodermatic dose. Morphine is also a useful palliative. If Cheyne-Stokes respiration occurs, inhalations of oxygen and carbon dioxide alternately, or one of them in its appropriate interval, may be helpful.

A Pharmacological Study of Cannabis Americana.—HOUGHTON and HAMILTON (*Therapeutic Gazette*, 1908, xxxii, 26) conclude a study of Cannabis americana (Canabis sativa) as follows: (1) The method for determining the physiological activity of Cannabis sativa by internal administration to especially selected dogs has been found reliable when the standard dose, 0.01 gram per kilo of body weight of the unknown, which is reduced to a solid extract, is tested on the same animals in comparison with the same quantity of a standard U. S. P. extract by an experienced observer. (2) Cannabis sativa, when grown in various localities of the United States and Mexico, is found to be fully as active as the best imported Cannabis sativa, as shown by laboratory and clinical tests.

Trypsin in the Treatment of Malignant Tumors.—GRAVES (*Boston Med. and Surg. Jour.*, 1908, clviii, 121) states that it cannot be claimed that any great advance has been made in the actual cure of cancer by the use of trypsin. Nevertheless, the scientifically established fact that trypsin has a specific destructive action on the cancer cell and on the deadly ferment which it secretes, gives at least a gleam of hope that an effective method of applying it may be discovered.

Sodium Anilarsenate in Trypanosomasis.—NAEGELI-AKERBLOM and VERNIER (*Therapeutischer Monatshefte*, 1908, xxii, 77) review the experiences of various observers upon the treatment of sleeping sickness and trypanosomiasis in animals, and conclude that sodium anilarsenate (atoxyl) is less effective in these conditions than some have believed. The drug is dangerous in large doses, sometimes causing gastric irritation, colic, vertigo, and even blindness. R. Koch advises its early use in trypanosomiasis, the diagnosis having been made upon the appearance of glandular swellings and upon the examination of the blood; he does not, however, consider the drug a specific. Sufficient dosage would seem to be 7½ grains every two days for a period of two months; this amount may be given hypodermatically. With regard to the employment of trypan-red the authors are not enthusiastic, stating that it acts less upon the parasite than upon the host.

Calcium Chloride in Hemoglobinuric Fever.—DEADERICK (*Therapeutic Gazette*, 1908, xxxii, 86) reports four instances of hemoglobinuric fever treated by calcium chloride, in which the results were not all that could have been desired. He concludes with the statement that the number of patients is too small to permit the drawing of definite inferences, but it would appear the benefits claimed by Vincent for the treatment were not obtained. Two of the patients died, and in both death was due to exhaustion resulting from the hemolysis, the very process which calcium chloride is used to combat. Deaderick considers the treatment worthy of further trial.

Salicylate Preparations in Bronchial Asthma.—VON GRESIC (*Klinisch-therpeautische Wochenschrift*, 1908, xv, 96) is accustomed to employ aspirin in all cases of bronchial asthma since he obtained a rather remarkable result in a patient who had suffered from the affection for many years and who experienced striking relief from a marked asth-

matic seizure following the administration of 15 grains of the drug; two hours after the first dose a second of equal size was given, after which the symptoms of the attack entirely subsided. Further attacks were treated in the same fashion and with considerable success. The aspirin seems to lessen the severity of the attack and to shorten its duration. In very severe attacks the addition of morphine is of advantage.

Treatment of Pleurisy with Effusion.—Barr (*Monthly Cyclopedia of Practical Medicine*, 1908, xi, 1) advises early removal of the fluid in its entirety, but before any negative pressure is established and before the patient feels any discomfort the siphon is stopped and an amount of air about equal in volume to the fluid withdrawn is introduced into the pleural cavity, then the remainder of the fluid is drawn off and a dram of 1 to 1000 adrenalin solution, diluted with about twice this amount of normal saline solution, is injected, and if it seems necessary more air is introduced to make the total amount equal to half or three-fourths of the bulk of the fluid withdrawn; the larger quantity of air is introduced in tuberculous patients. A siphon is preferable to an aspirator, because its force can be regulated and its negative pressure never exceeds 1 pound to the square inch. The adrenalin solution is introduced to contract the bloodvessels and to lessen the secretion, but its effect is not prolonged, and consequently it cannot be expected to lessen the secretion for any great length of time if there be a great negative pressure in the pleura. When the use of adrenalin is supplemented by the introduction of air, the negative pressure is lessened or abolished and the lung gradually expands as the air is absorbed.

Bismuth in Gastric Diseases.—Ruault (*Gazette médicale de Nantes*, 1908, xxvi, 114) perscribes bismuth subnitrate in 5-drachm doses in gastric pain (cramps, the pain of ulcer, cancer, and hyper- and hypo-acidity). The bismuth is given in a single dose in the morning and is suspended in about a pint of water. After taking it the patient lies for about ten minutes upon the back, each side, and upon the abdomen, and eats nothing for at least an hour. Constipation is not induced, the large doses tending rather to regulate the bowels. The treatment is of little avail in nervous dyspepsia, but is very effectual in gastrorrhagia and fermentative conditions. The bismuth has both a local and an antiseptic action; it soothes pain and protects ulcerations, lessens their tendency to irritation, favors cicatrization, and diminishes fermentation.

The Treatment of Pruritus Vulvæ.—Dalche (*La Quinzaine therapeutique*, 1908, viii, 505), in addition to treatment of the patient's general condition, institution of proper diet, the employment of calomel, if hepatic torpor is present, and hydrotherapeutic measures, especially the sitz bath in tepid running water, recommends various local applications, such as an ointment consisting of menthol, ¼ grain; guaiacol, 1 to 3 minims; zinc oxide, 2 drams; vaseline, 1 ounce. Ichthyol ointment is useful and very sedative in action. Powders are often effective also, especially orthoform, diodoform, and talcum. Local lesions, such as ulcerations, pustules, and the like, should receive appropriate treatment.

The Bromides in Epilepsy.—SPRATLING (*Albany Medical Annals*, 1908, xxix, 172) contends that the bromides have contributed nothing to the curability of epilepsy. If they are used at all they should not be given in doses to exceed 15 to 20 grains daily, and these amounts should be increased so slowly that bromism will not appear. It is unnecessary to cause bromic acne to get the physiological effects of the drug; 5 grains three times a day given on scientific principles is of far greater value than 20 grains at similar intervals given without heed to eliminative precautions.

The Influence of the Röntgen-rays upon Malignant Growths.—BECLERE (*La Revue médico-sociale*, 1908, ii, 13) gives the following conditions as influencing successful Röntgen-ray treatment: (1) A more or less deep situation of the different cellular elements of the tumor treated. (2) A variable degree of the sensibility of these elements to the action of the rays. (3) The rapidity of evolution of the growth or the more or less rapid multiplication of its cellular elements. (4) The integrity or the involvement of the vascular system and more especially that of the superficial or deep lymphatics of the region.

The Röntgen-rays in Sarcoma.—BABCOCK and PFAHLER (*Surgery, Gynecology, and Obstetrics*, 1908, vi, 160) state that the most potent single agent against sarcomatous growth is probably the *x*-rays. The rays have a destructive effect on all living tissue cells and an especially pronounced action against lymphoid and young connective tissue cells. Consequently the embryonic tissue of sarcoma is particularly vulnerable. The rays also increase the fibroconnective tissue in the area treated, and thus tend to produce a denser encapsulation of the growth and to obliterate adjacent lymphatic channels. There is no reason to believe that the rays increase the tendency to metastases. The technique should vary with the patient in hand. Usually in deep tumors the anode should be about 30 cm. from the skin; the exposure should average from twenty to fifty minutes, the application being divided between two different areas, the object being to have the rays enter from every possible direction. An old high vacuum tube is likely to give the best results, but with superficial lesions a lower and softer tube should be employed. In general, the rays measuring 6 to 8 (Benoist scale) will give best results. Usually 1 ma. of current is employed, as it is difficult to use a stronger current and keep the vacuum uniform. In protecting the skin the use of a diaphragm of sole leather interposed between the tube and skin is important. The treatment is given daily for months, or until the irritation of the skin or the disappearance of the neoplasm suggests increasing the intervals between the exposures. After apparent cure the treatment is kept up at intervals of from two to eight weeks for several years. At the outset the patient should be advised that the treatment will take a long time, and that the tendency to recurrence may only be overcome by occasional treatments for several years. The patients who show the greatest tolerance to the rays seem to do best.

PEDIATRICS.

UNDER THE CHARGE OF

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Cutaneous Reaction after Vaccination with Diphtheria Toxin.—B. SCHICK (*Münch. med. Woch.*, 1908, lv, 504) injected diphtheria toxin in various concentrations beneath the human skin to determine its reaction. After concentrating it to one-tenth its volume in vacuo at a temperature of 30°, he obtained a definite cutaneous reaction, which in appearance is identical with the reaction obtained after injecting tuberculin. Unless the operator knows which solution he injected, he cannot tell the difference between the two reactions. Clinically, the tuberculin reaction is not nearly so often associated with a central pustule as the diphtheria reaction; this pustule is not due to infection, since the toxin has been found perfectly sterile a number of times. The specificity of the reaction was proved by neutralizing the toxin with antitoxin in vitro and injecting this solution, without, however, producing a reaction. The same was true in all cases in which the toxin injections were preceded, by twenty-four hours, by injections of 1500 to 3000 units of antitoxin, thus immunizing the patient passively. If the antitoxin injection is made several hours later, the reaction is as often positive as negative. In cases in which the reaction followed upon the toxin-antitoxin injection it lasted but forty-eight hours, while after pure toxin injections it lasted 120 hours. This shows that the antitoxin influences not only the production of the reaction, but also the healing. Of 95 children ill with diseases other than diphtheria, 36 reacted positively, 59 negatively; of 55 ill with diphtheria, 52 reacted positively, 3 negatively. In the former instances the reaction was much less intense than in the latter. Shick explains the latter reaction by the individual predisposition of individuals toward diphtheria.

The Clinical Symptoms of the Cases of Epidemic Cerebrospinal Meningitis Admitted into Belvidere Hospital, Glasgow, during the Recent Epidemic.—Between May, 1906, and May, 1907, there were admitted to the wards of Belvidere Hospital, Glasgow, 128 bacteriologically verified cases of epidemic cerebrospinal meningitis; 55 were acute, 8 mild, 9 abortive, and 56 chronic. During the latter phase of the epidemic the cases were of a more acute type. There were 63 males, 65 females; 97 were below fifteen, 31 over fifteen years of age; of the former, 77 died, of the latter, 17; 17 of each sex recovered. W. DOW (*Lancet*, 1908, i, 768) has studied the cases collectively, and describes the symptoms thus: The symptoms of onset were usually sudden; headache, vomiting, and vertigo existed in most; sore throat preceded in many cases for several days. The physiognomy was very characteristic; cheeks flushed and even cyanosed, herpes at lips, suffused conjunctiva, rigid, stiff head and neck; Kernig's sign was nearly always present; stupor and less frequently delirium

followed the onset. The skin symptoms included flushing at the commencement of the disease, pallor in advanced cases; goose-skin in chronic cases; tâche cérébrale throughout the course of the disease. The true rash was rarely present; when present, it consisted of small hemorrhages, which persisted from three to four days; it resembled the purpuric rash, but disappeared quicker; a general petechial rash was noted in 27 cases, only 1 of which recovered. Herpes, chiefly about the angles of the mouth, as in pneumonia, occurred in about 20 per cent. of the cases. Of the symptoms referable to the nervous system, pain was the most constant; the occiput, the frontal region, and the top of the head were the most constant seats of the pain. Next in frequency were the nucha and the spine. The state of mind may be one of apathy, and from this through every gradation to coma; delirium, however, was not infrequent; it varied between simple muttering and mania; it usually ceased as the pain disappeared, and thus does not mean convalescence, but rather the beginning of a chronic state. Hyperesthesia of the skin was common and intense; contraction of certain muscles was present in all cases, being most common in the posterior muscles of the neck and trunk. The plantar reflex was exaggerated in acute cases before the onset of coma; Babinski's sign was never obtained; the knee-jerks were exaggerated in acute cases before coma set in, but were absent in chronic cases. There was rapidly progressing emaciation in all chronic cases, but there were no trophic lesions. Chronic hydrocephalus was fairly common after the twentieth day; optic neuritis was associated with this. Convulsions, polyuria, and difficulties in deglutition were associated with its beginning. Convulsions were frequent in cases in children under one year of age. The pupils were contracted in delirium, dilated in coma; hippus was frequently observed; strabismus was moderately common in all stages; nystagmus was commonly observed in acute cases, occasionally in chronic; retraction of the upper eyelids occurred in hydrocephalus. The middle ear and the central auditory system were frequently affected, but Weichselbaum's organism was never isolated from the purulent discharge. Deafness was common in all cases in which recovery took place, and improvement does not result even after recovery. Taste and smell were not affected. Acute cases had a temperature range from 102° to 104°; it continued thus without remitting throughout the illness, and rose or fell before death. The pulse-rate varied greatly; it was usually accelerated, but sometimes much slowed; it was little influenced by variations in temperature. The respirations were accelerated from the beginning, usually out of all proportion to the pulse; modifications of Cheyne-Stokes breathing were noted. Vomiting occurred frequently; the appetite suffered only during the first days of the disease; the tongue was usually fairly clean; the spleen was not enlarged; the bowels were constipated; in acute cases, and especially in many of the children, there was loss of rectal control. Albuminuria was rare; glycosuria was never found; nephritis did not develop; incontinence of urine was common, particularly in children. Arthritic pain was rare; it affected chiefly the wrists, knees, and ankles; Weichselbaum's organism was obtained from the joints in only 2 cases.

Grave Chorea and its Relation to Septicemia.—B. Sachs (*Medical Record*, 1908, lxxiii, 505) reports two cases of a form of chorea, in which

he considers the cause to have been a severe general infection. Chorea, like epilepsy, has become a generic term, and the cases of functional idiopathic chorea are becoming fewer every day; many have an organic basis, and quite a large number are purely infectious. Its possible infectious nature has been spoken of for the last thirty-five years, and in a number of instances microörganisms have been isolated from the blood and tissues of individuals whose death ensued in the course of chorea; in but few, however, have septic organisms been isolated from the blood of the living subject suffering from the chronic disorder. As organisms found postmortem may allow of different interpretations, it is very important, in every case of severe chorea, to make repeated blood examinations, so as to prove the presence or absence of bacteria in the blood of the patient during the earlier stages of the disease. The clinical symptoms of septicemic chorea may be summarized thus: Occurring chiefly among youthful individuals, a somewhat indefinite period of restlessness and slight twitching is followed by universal choreic movements; the jactitations are so severe that the patients have to be restrained; erosions appear all over the body; speech is difficult at an early stage, and later becomes impossible; this is due to the disturbance in the mechanism of speech and the mental condition, which may vary from mild stupor to active delirium; sleep is almost impossible, and requires large doses of hyponotics. Stupor and coma develop within a short time, and death usually supervenes shortly. High fever exists all through the condition, and a toxic erythema has been noted in the earlier stages. In Sach's first case blood examinations made during life demonstrated staphylococci; in his second case no organisms could be isolated. He suggests the following classification for chorea, omitting posthemiplegic chorea as having a definite organic basis: (1) Cases due to exhaustion of the nerve elements, no infectious cause being found; (2) cases associated with endocarditis, rheumatism, and fever; (3) chorea gravidarum; (4) senile and chronic chorea associated with arteriosclerosis, nephritis, and other degenerative changes; (5) septicemic chorea; for this group the bacterial origin has been proved without doubt. The prognosis is very grave and the treatment has thus far been unavailing.

Appendicitis during Childhood.—Appendicitis has been considered a graver and more fatal disease in children, not only by surgeons but also by pediatrists; this is due to the fact that appendicitis, like all other inflammations in children, undergoes suppuration much more quickly than in adults, and that the diagnosis is usually made much later, as children cannot localize the pain as readily; it is frequently considered a simple digestive disturbance. To help in the clearing up of the question of prognosis, W. NEUBERG (*Deut. Zeit. f. Chir.*, 1907, lxxxix, 375) has tabulated 82 cases from Kredel's clinic in Hanover, with the following results: There were 41 males and the same number of females; 9 were between one and five years of age, 32 between six and ten, and the remainder between eleven and fifteen. Abscess formation was noted in 21 cases, 19 of which were operated on, with one death; in the other two cases the abscess perforated into the bladder with recovery. Of 11 patients who developed peritonitis (in 7 the condition was diagnosticated before the operation), 10 were operated upon, with 9 deaths. Of 38

patients treated expectantly, 1 died, a case of diffuse peritonitis, in which an operation was considered a hopeless undertaking. Of the 82 patients, 46 had been admitted to the hospital, and of these, 9 died, while of the 36 seen in private practice only 1 died. Light cases of appendicitis are frequently diagnosticated as intestinal derangement in children, thus removing many cases from the statistics which would make the prognosis of the condition seem more favorable. The youngest patient with a circumscribed abscess was twenty-one months old; operation was followed by recovery. In 15 cases fecal concretions were noted. In 2 instances intestinal obstruction developed four weeks after the acute attack; the patients were respectively six and eight years old; both recovered after operation.

OBSTETRICS.

UNDER THE CHARGE OF

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The Anatomy of the Pelvic Floor.—FOTHERGILL (*Jour. Obst. and Gyn. Brit. Empire*, January, 1908) contributes a well-illustrated paper upon the anatomy of the pelvic floor. He analyzes the views of anatomists who have written upon this portion of the body, and concludes essentially as follows: The so-called ligaments of the uterus lie loosely upon the subadjacent structures and have no supporting action. The broad ligament is a small part of the mesovarium or mesosalpinx. The ureterosacral and ureterovesical folds are not capable of resisting downward pressure, as is the round ligament, which is also of vestigial structure. The action of the external muscular layer of the pelvic floor is that of a sphincter rather than that of a support. The intermuscular layer of the pelvic floor is the degenerated representative of the tail muscles in the lower animals, and has largely lost its muscular action. The lower part of the levator ani acts as an adjuvant to the sphincters of the rectum and vagina. The classical descriptions of the fascia of the pelvis should be abandoned, and the fascia should be regarded as the sheaths of the muscles, the vessels, and the viscera. The internal muscular layer with its fascia forms the funnel-shaped pelvic diaphragm. This does not support the pelvic organs by its muscular action, and by virtue of its shape could not support the pelvic organs if they were not firmly attached to its sloping lateral walls. This attachment is accomplished by the fibrous sheaths of the blood-vessels and accompanying structures which supply the pelvic viscera. The most important cause of prolapse is relaxation of the perivascular sheaths. The attachments of the rectum to the back of the pelvis are distinct from the attachments of the urinogenital organs to its sides. The rectum does not descend with these organs when prolapse occurs. When the anterior rectal wall descends, forming a rectocele, it is united with the posterior vaginal wall by scar tissue, which is the result of infection during the healing of tears in the perineum.

Cerebral Hemorrhage during Pregnancy.—JARDINE (*Jour. Obst. and Gyn. Brit. Empire,* January, 1908) reports the case of a woman eight months advanced in her third pregnancy. She had lost two children previously from premature labor at the seventh month. During the present pregnancy her health had been good, aside from excessive apprehension lest the child should die. She was suddenly taken with loss of power in the right hand, twitching of the face, and unconsciousness. On admission to the hospital the pupils were equally and closely contracted and reacted to light. The right arm was very rigid, flexed at the elbow, with the fingers clinched in the palm. The second aortic sound was accentuated, the urine contained albumin, the patient was very restless, and the fœtal heart could not be heard. The pelvis was contracted and the os admitted two fingers. The vertex of the child was presenting. The patient continued to be unconscious, and labor gradually developed painlessly until dilatation was complete. As there seemed to be no strain upon the heart and bloodvessels, and the fœtal heart could not be heard, no interference was practised. A further cerebral hemorrhage occurred, manifested by stertorous breathing and loss of sensation, the limbs becoming limp. The patient died about two hours after the second hemorrhage. An autopsy could not be obtained.

Osteomalacia Treated by Section at Term, with Removal of the Uterus and Ovaries.—JARDINE (*Jour. Obst. and Gyn. Brit. Empire,* January, 1908) reports the case of a woman in her fifth pregnancy sent to the hospital in labor. She was suffering severely, her pulse being about 130 to the minute. The abdomen was greatly distended and pendulous and the skeleton considerably deformed. The pelvis was beak-shaped, the ribs softened, and the bones of the limbs very tender to the touch. The child was in breech presentation. The pelvis was so highly deformed that it was necessary to deliver the patient by section, which was followed by hysterectomy with intraperitoneal treatment of the stump. On section, the beaked condition of the pelvis could be seen very plainly. Mother and child made a good recovery. The osteomalacia present seemed to be completely arrested by the operation.

Toxemia during Pregnancy, with High Temperature.—JARDINE (*Jour. Obst. and Gyn. Brit. Empire,* January, 1908) reports the case of a primigravida who, after influenza, had cough with vomiting, intense colic in the epigastric region, the influenza being followed by a pneumonia at the base of the left lung. When this subsided the patient became jaundiced, vomiting became worse, and the patient lost in weight. When admitted to the hospital her pulse was 130; temperature, 101° F. She was much emaciated, the tongue was dry and clotted, there was bleeding from the gums, the urine was deeply stained with bile, and considerable anemia was present. Shortly after admission to the hospital the patient had a chill, with tenderness over the gall-bladder. No tubercle bacilli could be found in the urine or sputum, and the Widal reaction was negative. A dead child was extracted by forceps, the liquor amnii and membranes being deeply bile stained. The placenta was normal. After delivery the patient's temperature fell, her general condition rapidly became normal, and she ultimately made a good recovery.

Stab Wound of the Fœtus in Utero.—STEELE (*Surg., Gyn., and Obst.*, March, 1908) reports an interesting and rare case in which the fœtus in utero received an extensive stab wound. The mother, in a fit of anger stabbed herself with a knife in the right side of the abdomen, four inches to the right, and one and a half inches below the umbilicus. She was six and a half months pregnant. She was taken to the hospital and treated for one week, when the wound in the abdominal wall healed, and she returned home in good health. She was afterward delivered by a midwife of a living male child, fully developed, but having in the lateral aspect of the abdominal wall on the left side, one and a half inches above the anterior superior spine of the ileum, a mass of intestine the size of a closed fist. The child was immediately brought to the hospital for operation. On examination, a partially healed wound, one inch in length, was found. This wound had penetrated the abdominal cavity, and protruding through the wound, but not adherent to its margins, was the jejunum, the ileum, and all of the colon down to the sigmoid flexure. The upper part of the jejunum was enormously dilated, while the lower portion of the ileum and colon were coiled in an adherent and contracted mass. Meconium was found in the rectum. There were many firm adhesions around the margins of the wound, which entirely closed the peritoneal cavity. A transverse incision was made across the abdominal wall and the cavity entered with difficulty. On examination, the greater part of the intestinal tract was found outside of the abdomen agglutinated in the folds of the mesentery and omentum, and a plastic exudate. The entire mass was carefully restored to the abdominal cavity after the stomach had been catheterized through the œsophagus, and an effort had been made to introduce the tube through the rectum. To make the reduction, the child was held by the heels, with the head downward, and the edges of the wound were widely separated. The adhesions were so dense that one could not accurately recognize the condition of the intestine. The child survived the operation eight hours, and upon autopsy it was found that the jejunum had been completely cut across by the stab wound which penetrated the right abdominal wall of the mother, the right wall of the pregnant uterus, and the left abdominal wall of the fœtus. It is extraordinary that a stab wound through the abdominal wall of the mother, which wounded the child, should not have interfered with the growth of the child in the uterus, nor seriously affected the recovery of the mother. The two divided ends of the intestine were completely occluded by adhesions, and nearly three ounces of glairy sanguinolent fluid was found in the stomach of the infant.

Hematuria in Pregnancy.—BALLOCH (*Surg., Gyn., and Obst.*, March, 1908) reports the case of a multipara who had lived in a malarious region, and who at one time had expectoration of blood. Four years previous to coming under observation the patient passed blood in the urine. This occurred during pregnancy, and lasted ten days. During the next pregnancy there was no hematuria, but in the last pregnancy hematuria appeared and continued until the birth of the child. It varied in intensity and never entirely ceased. There was no history of renal colic. During the past year the patient has suffered from heaviness

and stiffness in the left side under the ribs, with soreness upon manipulation. Swelling of the feet had been constantly present since the first pregnancy. On examination, the urine contained abundant red blood cells, but no casts. On cystoscopic examination the bladder and ureters were normal, and bloody urine was seen to come from the left ureter. The left kidney was removed, and found to have two patches of subcapsular hemorrhage. There were dense adhesions above the upper pole, which had to be divided before the kidney could be removed. The patient made a good recovery, and pregnancy supervened, and again blood appeared in the urine. After the birth of the child the hematuria ceased. On examining the kidney, glomerulonephritis was present, with increase in the interstitial connective tissue seen upon cross-section of the pyramids. A study of the cases, treated by operation, shows that hematuria has ceased with equal promptness after decapsulation, nephrotomy, or nephrectomy.

GYNECOLOGY.

UNDER THE CHARGE OF

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Ovarian Hematoma.—E. H. WOLF (*Arch. f. Gynäk.*, 1907, lxxxiv, 211) reports 8 cases of ovarian hematoma, 4 of which were associated with myomas. 1 was met with in a case of general and peritoneal tuberculosis, and 3 were complications of pelvic peritonitis. In no instance was the diagnosis made previous to operation. Dysmenorrhœa and menorrhagia were the only symptoms constantly associated with this condition. The symptoms, as a rule, were obscured by those of the principal conditions—myomas, peritoneal tuberculosis, and inflammatory diseases of the appendages.

The Pathological Changes Affecting the Endometrium.—A Contribution toward their Classification.—ELIZABETH H. B. MACDONALD (*Jour. Obst. and Gyn. Brit. Empire*, 1908, xiii, 3) strongly favors routine examination of endometrial scrapings, as it throws interesting light on the manifold changes, physiological and pathological, of the endometrium. She examined scrapings from between 200 and 300 cases, and has from that work concluded the following classification to be the best to be followed in such study: First, conditions arising from decidual and fœtal retention which includes (*a*) simple cases, such as simple inflammatory reaction and (*b*) the malignant type as chorioepithelioma. Second, endometritis of infective origin. This class is subdivided into the acute and chronic classes. These conditions may be considered as being puerperal, gonorrhœal, syphilitic, tuberculous, or septic—from operative procedures, etc. Third, secondary changes, as (*a*) chronic œdema which embraces mucous polypus and (*b*) general

hyperplasia; chronic venous congestion, and (*c*) increased vascularity. Her fourth and last class is that of new growths. These may be of a simple character of glandular overgrowth, such as (*a*) simple adenoma or papilloma; (*b*) papillary glandular hyperplasia; and (*c*) stroma overgrowth; or of a malignant type, as (*a*) malignant adenoma, (*b*) adenocarcinoma, (*c*) sarcoma. MacDonald's general conclusions are that the endometrium is to be regarded as an unstable tissue, subject to great physiological variation, readily affected by disorders of neighboring tissues, readily responsive to stimulation, but only rarely the seat of primary disease. Malignant disease of the body of the uterus is comparatively rare; simple tumor formation is uncommon; chronic infective endometritis is commoner than these, but still not common by comparison with the number of other conditions for which curetting is practised. In the great majority of the cases in which the uterus is scraped the endometrium has played a merely passive part in the pathological changes, although its removal may be a justifiable and even necessary part of the treatment.

Solid Ovarian Tumors.—Briggs (*Jour. Obst. and Gyn. of Brit. Emp.*, 1908), during the past twenty-one years, has operated for ovarian tumors in 488 cases, in 49 of which the tumors were solid. The 439 cystic tumors were divided as follows: 284 adenocystomas, 44 dermoids, 36 broad ligament cysts, 24 papillomas, 50 carcinomas, and 1 perithelioma (sarcoma). Of the 49 solid tumors, 31 were fibromas, 1 cellular spleen-like tumor, 3 fibromas of the ovarian ligament, 1 surface papilloma, 3 adenomas, 8 solid carcinomas, 1 solid teratoma (myxochondrosarcoma), and 1 round-cell sarcoma. Walker, studying this material, was impressed by the rarity of sarcoma, having found but one specimen among the 439 of cystic tumors removed. He found 50 carcinomas (1 in 9), and among the 49 solid tumors he found 8 carcinomas (1 in 6), making 58 of 488 ovarian tumors, or 1 in 8.4. Veit gives this proportion as 1 in 5.5 and Martin, in 236 cases, found it was 1 in 7.3. In the 488 cases of ovarian tumors sarcoma was found in but 3 cases (1 cystic and 2 solid). The proportion of sarcoma to carcinoma was 3 to 58, about 5 per cent. In the solid variety the proportion was 1 to 4, while in the cystic it was but 1 to 50. It may possibly be found that more sarcomatous involvement of the cystic growths will be discovered by a careful analysis of the 36 specimens classed as broad ligament cysts, inasmuch as sarcoma frequently invades ovarian cysts so situated. In considering the solid tumors, it is interesting to note that the fibromas were found in 31 of the 488 cases, that is, in 6.3 per cent. of all the cases. This is notably in excess of the usual estimate of 2 per cent. This however, may be due, at least in part, to Walker's inclination to regard as fibromas many that others might decide to be sarcomas. In this Walker seems to be supported by the subsequent clinical history of the patients. Apropos is quoted this paragraph: "Dr. Briggs was amongst the first to recognize that even the highly cellular connective tissue tumors of the ovary were not necessarily sarcomas; the after-histories of 8 cases of fibroma of the ovary and 1 case of fibroma of the ovarian ligament were then produced, the structures of the growths were described and illustrated. They, together with cases of Doran

and others, formed the basis of a paper in support of the conclusion that solid, heavy primary tumors of the ovary were probably fibromas and not sarcomas." It is quite remarkable that 31 of the 49 solid tumors were fibromas and yet not one fibrocystoma was found among the 439 cystomas. Walker found the circumscribed ovarian fibroids were 9 in number, while 15 were diffuse and 7 pedunculated. In but 2 instances were the tumors bilateral. The pedunculated were usually larger than the circumscribed, as were the diffuse. Of the 8 cases of solid carcinoma, 7 were bilateral and secondary and 1 primary and unilateral. Ascites was present in 12 cases of fibroma and absent in the 3 cases of fibroma of the ovarian ligament. It was present with the surface papilloma and with 5 of the 8 solid carcinomas, with the solid teratoma and the round-cell sarcoma. When adhesions were universal it was always absent.

Parasitic Uterine Myomas.—T. S. CULLEN (*Jour. Amer. Med. Assoc.*, 1907, xlix, 1995) mentions several specimens of uterine fibroids that had become absolutely detached from the uterus and had acquired new sources of blood supply and given this name. The mesenteric vessels, the omentum, the bladder, the bowels, and the Fallopian tube have each thus acted as foster-mother for these growths. When the omentum is thus acting its bloodvessels are noted to be much enlarged, the fat is removed, and even the lymphatics take on hypertrophy.

Superficial Papilloma of the Ovary.—E. EMRYS-ROBERTS (*Jour. Obst. and Gyn. of Brit. Emp.*, 1908, xiii, 96) reports a case of this very rare disease. The woman, aged forty-seven years, had been married twenty-six years and had been pregnant once, which terminated in a full-term labor twenty-five years ago. For four months she had noticed swelling of the abdomen. The last two menstrual periods had been profuse. At operation a secondary growth was found in the peritoneum at the line of incision. The primary tumor was a large mass filling the pelvis. The opposite ovary presented numerous surface adhesions; it was enlarged to the size of a bantam's egg; on section it exhibited numerous follicles distended with altered blood. Several corpora lutea were present. A small psammomatous mass was attached to the right ovarian fimbria. The right ovary was completely hidden by a luxuriant papillomatous growth the size of a Jaffa orange; many of the papillæ were cystic and were distended with a clear fluid; a few psammoma bodies, the size of peas, were scattered throughout the growth. On section, the ovary was seen to be of normal size, and apparently in full functional activity. The whole of its external surface, with the exception of the hilum, gave origin to the papillomatous newgrowth. A microscopical section of the right ovary at a point where the tumor was typical, showed a normal condition of the ovary, except near the periphery where the stroma assumed a denser form, which is particularly associated with papilloma of the ovary, whether of the intracystic or superficial variety. The normal portion displayed the usual characters of a functionally active ovary. At one portion of the section the dense stroma near the periphery contained numerous acini lined by a single layer of epithelium, cylindrical in type, with deeply staining nuclei; this resembled in every particular the germinal epithelium, and thus

demonstrated these acini to be ingrowths. The germinal epithelium also showed outgrowths or papillæ, each containing a core of dense fibrous stroma, which latter was seen to be undergoing serious degenerative changes in the larger ones. Emrys-Roberts concludes that primary superficial papilloma of the ovary is derived from the germinal epithelium and underlying connective-tissue stroma, that the vesicles so common result from papillæ whose cores have undergone œdematous degeneration, that secondary deposits arise from disrupted papillæ, and that the dissemination of secondary deposits is favored by ascites. And, further, that the ascites represents the secretion of the epithelium forming the outer covering of the growth.

OTOLOGY.

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The Diagnosis and Differential Diagnosis of the Vertigo of Meniere.—FRANKL-HOCHWART (*Archiv. f. Ohrenheilk.*, 1907, lxix, 233) makes two divisions of the cases presenting the complex of symptoms first described by Ménière, the apoplectic and the accessory; the former includes persons of previously normal hearing who become suddenly deaf, in one or both ears, and in whom the loss of hearing is accompanied by circulatory tinnitus, vertigo, nausea and vomiting; the later includes cases of vertigo, more or less pronounced, consequent upon changes incident to both acute and chronic processes, in the middle ear or labyrinth, and but rarely associated with diseases of the external ear or auditory nerve. In addition to these two main classifications it is necessary to consider the pseudo-Ménière attacks exhibiting the whole, or parts, of the symptom series, as observed in the neuroses or as aura of hysterical or epileptic attacks.

The prominent symptoms of the labyrinthine hemorrhage of Ménière are the excessive vertigo, loss of hearing, distressing tinnitus, ataxia, nystagmus and vomiting and, in some instances, in addition, brachycardia, later tachycardia, diarrhœa, sense of pressure in the head and dimness of vision. The diagnosis which is easily determinable by this array of symptoms is rarely evidenced between the attacks by any objective signs, the total loss of hearing being the main persistent indication of the causative accident.

In the accessory vertigo resulting from cerebral apoplexy, vertigo, and vomiting are frequently associated symptoms but in apoplexy of the labyrinth consciousness is rarely lost and there are lacking the paralyses, the aphasia, the hemianopsia and correlated symptoms which indicate a central lesion. In apoplexy of the labyrinth there is monaural or binaural loss of hearing, in cerebral apoplexy the hearing may be unaffected or there may be a temporary phonophobia.

The diagnosis of the cause of accessory vertigo is especially difficult when the examination is made between paroxysms; if there is no marked impairment of hearing a vestibular cause for the vertigo is unlikely, though it cannot be entirely excluded; when the hearing is greatly impaired a vestibular participation is probable, though very deaf patients may be subject to vertigo of purely extrinsic origin.

The vertigo accompanying oculomotor paralysis has little resemblance to that of apoplexy of the labyrinth, in the latter instance the patients sometimes complain of double vision but this is usually found on investigation to be rather a variability of vision with vague apparent movement of the objects seen; the vertigo accompanying refraction anomalies is wanting in the definiteness of direction of that excited by a lesion of the semicircular canals.

In all cases of vomiting, when the culpability of the digestive apparatus is questionable, an examination of the ear should be made, as likewise in cases of arteriosclerosis in which the vertigo assumes definiteness of direction; in these cases vomiting is rare though the circulatory tinnitus is sometimes excessive.

In cases of brain tumor the differential diagnosis is less difficult than might be supposed, the vertigo is usually severe and frequently accompanied by nystagmus and vomiting but tinnitus is rare and other symptoms, papillitis, paralyses, and psychic anomalies, which are not accompaniments of labyrinth lesion, usually present themselves; headache, according to the author, is an almost constant accompaniment of labyrinth apoplexy but never reaches the grade of severity characteristic of brain tumors.

In the differential diagnosis, in cases of suppurative middle-ear disease, between the vertigo of extrinsic, or middle ear, causation and that accompanying meningitis or cerebral abscess the vertigo in the latter instances is, according to the author, a less typical vertigo accompanied by tinnitus than a general vertigo, the true origin of which must be sought through the medium of ophthalmoscopic examination, lumbar puncture, and other investigating measures.

The vertigo of the neurasthenic is rarely typical in its manifestations and nystagmus is not an accompanying symptom. In hysteria and in epilepsy the diagnosis is often difficult on account of the masking symptoms and the fact that a simulatively typical series may occur with normal hearing, this relation of symptoms is rare in hysteria, the objective examination furnishing the clue to the real condition, while in epilepsy the diagnosis is determined by the convulsions, loss of consciousness, and other evidences of the true nature of the attack of which the pseudotypical symptoms are the aura.

Especially to be distinguished from the vertiginous paroxysms accompanying the presence of basal tumors is the cerebral polyneuritis with typical symptoms, first described by the author, in which there is acutely incident loss of hearing, vertigo, tinnitus, vomiting, accompanied by facial paralysis and herpetic eruption, but in which the prognosis is good for ultimate complete recovery.

Adenoid Vegetations and Impairment of Hearing.—Cohn (*Zeitschrift f. Ohrenheilkunde*, v. lii, p. 246). As an argument for the establishment of exact examination of the nose, throat, and ears in school

children the author gives the result of his investigations in 1573 cases. Of this number 315, or about 18 per cent., were found to have a sufficient degree of impairment of hearing to make a professional examination advisable, although in the majority of them the impairment had not been noticed, either by the patients themselves or by the teachers. In 153 cases the impairment of hearing was directly referable to the presence of adenoids, and in 12 additional cases it was referable to the consecutive changes induced by adenoids which had spontaneously resolved. The number of cases in which adenoid vegetations could be regarded as the causative factor in the impairment of hearing in all the cases considered amounted therefore to about 52 per cent., and the author lays stress upon the importance of a preliminary examination of all school children, both objectively and by hearing tests, at their entrance upon school life, as well as at later stated intervals, and gives the Bezold estimate of 2 metres, for the whispered voice, as the lowest acceptable standard.

On Some Uses of Peroxide of Hydrogen in Diseases of the Ear, Nose, and Throat.—LAMB (*Folia Therapeutica*), October, 1907. In subacute and chronic suppuration of the middle ear peroxide of hydrogen is a useful application, acting, in the opinion of the author, not only as a disinfectant and deodorizer, but also, to some extent, as an astringent; furthermore its active effervescence, in contact with blood or pus, exercises a mechanical action which helps in the breaking up of masses of septic material and the detachment of epidermal scales, cleaning a septic ear better than any preparation with which the author is acquainted, and this without signs of irritation when used in the ten-volume strength of a pure preparation. When discharge from the ear is profuse the discharge should first be washed away by syringing with warm, boiled water, and the ear then filled with a cold solution of the peroxide. At the conclusion of effervescence the ear should again be syringed and dried, and appropriate applications made. In mastoid operations the author has found the peroxide of value in cleansing foul cavities and also in checking the profuse oozing from small vessels, the mopping of the wound being done with small strips of sterilized lint soaked in the peroxide. This solution has also been found to be serviceable in the loosening of the gauze packing in post-operative dressings, as, for instance, in the first dressing after a radical operation.

HYGIENE AND PUBLIC HEALTH.

UNDER THE CHARGE OF

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Tuberculosis of Alimentary Origin.—A. CALMETTE and C. GUERIN (*Ann. de l'inst. Past.*, 1907, xx, 353) infected four cows with tuberculosis by introducing virulent bovine bacilli into the second and third

stomachs by means of a stomach tube. All of the subjects acquired pulmonary tuberculosis without the development of any lesions in the alimentary tract. Calmette and Guerin believe that whereas tubercle bacilli are retained in the mesenteric glands of young animals often for long periods, with ultimate healing, and since this defence is less efficient in the case of adult animals, the so-called primary pulmonary tuberculosis of the adult is most often of intestinal origin. In a later paper (*ibid.*, No. 8, p. 609), in which the literature of the subject is extensively reviewed, Calmette and Guerin announce their conclusion, drawn from their studies and experiments, that the vast majority of cases of pulmonary tuberculosis are due to bacilli introduced primarily into the alimentary tract, and that single intestinal infections produce a mild form of the disease, during the course of which the animal reacts to tuberculin for a period of one or two months, and then frequently recovers.

According to WEBER (*Deut. med. Woch.*, December 6, 1906) infection of the human subject with bovine bacilli is of vastly less importance than that due to those of human origin. It produces only intestinal and mesenteric lesions which point to the food as the vehicle of the exciting cause; these forms of the disease are much less likely to be transmitted from one victim to another. But inasmuch as bovine infection of the human subject is a real danger, all proper precautions should be taken to prevent its occurrence through foods and notably milk.

From a study of 4000 cases of pulmonary tuberculosis, including 700 which came to autopsy, N. RAW (*Lancet*, March 2, 1907) divides tuberculous infections into two groups: (1) Those due to bacilli of the human type. (2) Those due to bacilli of the bovine type. Under Group 1 are included phthisis pulmonalis, secondary ulceration of the intestines, and tubercular laryngitis; under Group 2 are included acute miliary tuberculosis, primary intestinal and mesenteric disease (tabes mesenterica, tuberculous peritonitis, tuberculosis of the pelvic organs), tuberculous lymphatic glands, tuberculous joints and bones, lupus, tuberculous meningitis, and tuberculous ulceration of the cornea.

In the Children's Hospital, Leipzig, H. BRUNING (*Abst. Hyg. Rund.*, November 15, 1906, p. 1257) found evidences of tuberculous lesions in 44 of 400 cases which came to autopsy, that is to say, in 11 per cent. Of these subjects one-fourth were infants. Tuberculous bronchial glands were found in 34 (77 per cent.); the liver and mesenteric glands were found diseased in 25 (57 per cent.); the small intestine in 20 (45 per cent.); and the large intestine in 10 (23 per cent.). General miliary tuberculosis was found in 25 cases. In 8 cases there was evidence of tuberculous infection of the intestines and mesenteric glands alone, and these must be considered as primary infections. In not one of these cases had tuberculosis been diagnosticated during life and all of the victims had died of some acute infectious disease.

A. EBER (*Zeit. f. Fleisch. u. Milchhyg.*, xvi, 1906, Nr. 7, p. 218) inoculated a bovine animal with material from tuberculous human mesenteric glands, and then from this animal reinoculated another, which succumbed to acute miliary tuberculosis within a week. By passing the material through a guinea-pig first, and then inoculating a bovine animal, death resulted in fifty-one days.

L. RABINOWITSCH (*Berl. klin. Woch.*, 1906, Nr. 24, p. 284) has summed up her observations on human and bovine tuberculosis and believes that the bovine variety does cause tuberculous lesions in man, but what proporton of cases are due therto cannot be determined.

H. VALLEE'S (*Comp.-rend. Acad. sci.*, cxlii, 1906, No. 20, p. 1101) studies incline him to the belief that in many cases of moxt extensive tuberculous involvement of the lungs and bronchial glands the initial lesion is in the intestine and due to tuberculous material in the food.

The same authority (*Comp.-rend. Soc. biol.*, 1906, lx, No. 19, p. 911) finds that normal-appearing mesenteric and other lymphatic glands of cattle may harbor virulent tubercle bacilli after infection from any source. We cannot conclude, therefore, that any of the lymphatic glands of a tuberculous animal are free from bacilli; hence, the importance of rejecting meat from diseased cattle.

Raw versus Sterilized Milk.—BRUNING (*Zeit. f. Tiermed.*, 1907, x) has carried out some experiments which help to demonstrate how complex is the question of the comparative value of raw and sterilized milk in infant feeding. A litter of newborn animals was divided, and part were fed with raw and part with boiled milk of another species; the latter fared the better. On the other hand, animals fed on raw milk of their own species did better than those that received it cooked. BOHME (*Deut. med. Woch.*, October 25, 1906) made comparative tests with milk treated with hydrogen peroxide and perhydrase and sterilized milk. The former agrees well with infants more than three months old; but with those younger than that sterilized milk gave the better results. It is to be said, however, that the number of infants under observation was far too small to warrant much generalization.

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INDEX.

A

Abdominal Cesarean section, relative indications for, 704
colpopexy for prolapsus uteri, 151
herniæ, 761
operations, 758
section for irreducible retroversion and retroflexion of the pregnant uterus, 147
tumors, diagnosis of, 605
Abortion produced by Röntgen rays, 617
rupture of cervix in, 772
Abscess formation, 758
Absence and marked diminution of the hydrochloric acid of the gastric contents in cancer involving organs other than the stomach, 132
Acetabular epiphysis of femur, separation of, 291
Acetone bodies, 754
in treatment of inoperable carcinoma of uterus, 774
Acetonemic conditions in children, 143
Acne vulgaris, treatment of, 142
Actinomycosis of appendix, 289
Action of oil in gastric acidity and motility, 753
Adams-Stokes disease, 155
Adenoid vegetations, 923
Adiposis tuberosa simplex, 325
Adolescent coxa vara, 291
Adrenal gland, tumors of, 871
Adrenalin-saline solutions in treatment of lowered blood pressure in peritonitis, 136
Affections of liver and spleen, diagnosis of, 287
Air, sewage bacteria in, 468
Airol, 153
Alburger, H. R., chorio-epithelioma of uterus, 412
Alcohol in gastric diseases, 764
Alcoholism, 156
Allen, A. R., symptom complex of transverse lesion of the spinal cord and its relation to structural changes therein, 735
America, pubiotomy in, 771
Amœbic dysentery, ipecacuanha in, 764
hepatitis, presuppurative stage of, 130
Amyxorrhœa gastrica, 207
Anaphylaxis, review of, 777
Anders, J. M., adiposis tuberosa simplex, 325
Anemia, bothriocephalus, 285
pernicious, 285
Anesthesia, scopolamine-morphine, 770
spinal, 133
Aneurysm of aorta, 515
of internal carotid artery, 464
of thoracic aorta, value of blood pressure determination in diagnosis of, 601
Angina pectoris, treatment of, 909
Ankylostoma duodenale, hemolytic action of, 903
Anspach, B. M., chorio-epithelioma of uterus, 412
Antidiphtheritic serum in general therapeutics, 453
Antiferment of the blood, influence of, on the proteolytic leukocyte ferment, 600
Antineoplastic serum in cancer, 452
Antitoxin in diphtheritic paralyses, 298
Antituberculosis serum and the tubercle bacillus, 610
Aortic insufficiency, pulse and blood-pressure changes in, 752
Appendages, inflammatory diseases of, surgical treatment of, 460
Appendices epiploicæ, torsion of, 864
Appendicitis, acute, 759
and gastric ulcer, 757
catarrhal, 290
chronic adhesive, 450
during childhood, 915
relation of traumatism to, 294
Appendix, actinomycosis of, 289
Appendix, carcinoma of, 702, 822, 851
Arnold, H. D., importance of the early detection of aneurysm of the aorta, 515
Arrhythmia, cardiac, 534, 778
Arsenic in treatment of syphilis, 139
Arteriosclerosis in the young, 199
nervous manifestations of, 187
treatment of, 141
Arthropathy in rötheln, 146
Artificial vagina, formation of, by intestinal transplantation, 461
Arthritis deformans, pyroligneous acid in, 141
Ashhurst, A. P. C., perforation of the gall-bladder during typhoid fever, 541
Aspermia, 293

Aspiration drainage in treatment of empyema, 64
Aspirin in asthma, 763
in emphysema, 763
Asthenozoöspermia, 293
Asthma, bronchial, 910
Autogenous vaccines in therapeutics, 755
Auto-intoxication, neurasthenia of, 558
Axial rotation of pedicle in tumors of ovary, mechanism of, 305
Azoöspermia, 293

B

Bacilli of tuberculosis, 584
Bacteria, sewage in air, 468
Bacterial diseases, vaccine therapy in, 765
vaccines in therapeutics, 451
Bacteriological infection of urinary tract in childhood, 611
Bacteriology of meningitis, 613
Banti's disease, splenectomy for, 604
Bartlett, F. H , epidemiology of acute poliomyelitis, 647
Bone formation in human penis, 293
transplantation in extensive defects of continuity in long bones, 290
histological studies on, 757
Bothriocephalus anemia, 285
Bovée, J. W., suppurative phlegmonous gastritis, 662
Bier, method of, in treatment of middle ear disease. 308
Biliary passages, infections of, diagnosis and treatment of, 37
Bismuth subnitrate in gastropathies, 296
Bladder, rupture of, 303
Blindness in Portugal, 153
Blood pressure in healthy athletes, effects of prolonged and severe exertion on, 131
Bloodgood, J. C., clinical and pathological differential diagnosis of diseases of the female breast, 157
Breast, female, diseases of, 157
Breech presentation, 770
Brewer, G. E., operations on the kidneys and ureters, 625
Briggs, W. A., torsion of appendices epiploicæ and its consequences, 864
Bunting, C. H., chronic fibrous myocarditis in progressive muscular dystrophy, 244

C

Calcareous fibromyoma of right ovary, labor complicated by, 459
Calcium chloride in therapeusis, 607
Caloric value of modified milk in its relation to infant feeding, 767
Cancer, antineoplastic serum in, 452
Cancer infection, 294
operations, 294
recurrence, 294
Cannabis Americana, study of, 910
Carbolic acid in diseases of skin, 621
Carcinoma, healing of, by sunlight, 622
of mediastinum simulating aneurysm, 529
of ovary, 150
of uterus, inoperable, 774
of vermiform appendix, 702, 822, 851
of vulva, 775
splenectomy for, 603
Cardiac arrhythmia, 534
experimental, 778
disease, vasodilators in, 607
dyspnœa, morphine in, 297
Cardiovascular-renal disease, 1
Carotid, common, ligation of, 760
Castration, bilateral, internal hemorrhages after, 772
Catarrhal appendicitis due to presence of oxyuris vermicularis, 290
Cauda equina and lower vertebræ, tumors of, 365
Cerebrospinal meningitis, epidemic, in Belvidere Hospital, Glasgow, 913
etiology of, 215
in Hartford, Connecticut, during 1904–1905, 351
practical importance of sore throat in epidemic, 299
purulent, 240
serum-treatment in, 902
Cervix, rupture of, in abortion, 772
uteri, chondrosarcoma of, 307
Cesarean section, abdominal, relative indications for, 704
for unusual indications, 769
uterus four years after, 304
Cheney, W. F., diagnosis and treatment of the gastric neuroses, 25
Cholecystectomy, 536, 541
Cholecystitis and cholelithiasis, 759
Cholelithiasis and cholecystitis, 37
Cholesteatoma, spontaneous operation induced by, 309
Chondrosarcoma of cervix uteri, 307
Chorea and its relation to septicemia, 914
Chorio-epithelioma complicated by hematometra, 459
of uterus, 412
outside the uterus and primary embolic chorio-epithelioma of vagina, 458
Chronic fibrous myocarditis, 244
Cirrhosis of liver, tuberculous, 779
Clark, L. P., curability of a rare form of nocturnal petit mal by the use of large doses of bromide, 94

Claytor, T. A., etiology and symptomatology of cerebrospinal meningitis, 214
Collins, J., some fundamental principles in the treatment of functional nervous diseases, 168
Colloidal metals in infections and especially in pneumonia, 451
Compensatory venous congestion, 441
Concretion in the lymphoid mass at the vault of pharynx, 463
Congenital adhesions in the common iliac veins, 342
Congestion, venous, 441
Conner, L. A., clinical study of heart cases, 790
Cough, nasal, 465
Convulsions, infantile, 296
Coxa valga and its varieties, 905
Coxa vara, adolescent, 291
Crane, A. W., specific immunity and *x*-ray therapeutics, 420
Creosote carbonate in bronchial and pulmonary affections in infants, 607
Curability of a rare form of nocturnal petit mal by the use of large doses of bromide, 94
Cyanosis, microbic, observations on, 442
Cystocele, 461
operation, a simplified, 462
Cystoscopic findings in vesicovaginal fistula, 461

D

Deaver, J. B., diagnosis and treatment of the biliary passages, with especial reference to cholelithiasis and cholecystitis, 37
some of the reasons why cholecystectomy should not be performed as frequently as is advocated by many surgeons, 536
Deciduoma malignum, 146
Diabetes mellitus, nature and management of, 508
new treatment for, 609
paralysis of accomodation in, 776
potatoes in, 763
santonin in, 609
Digalen, advantages of, over other digitalis preparations, 141
Digitalis and glyceryl nitrate, absorption of, 451
prolonged administration of, 609
use and abuse of, 781
Diller, T., pontile hemorrhage, 408
Diphtheria, pharyngeal, 145
toxin, cutaneous reaction after vaccination with, 915
treatment of, in young children, 457
Diphtheritic paralyses, antitoxin in, 298
Diseases and displacement of testicle in childhood, 299
Dixon, S. G., reaction of the phagocytes of elephant's blood on the bacilli of tuberculosis, 584
Dupuytren's contraction, surgical aspects of, 856
Dyspnœa, cardiac, morphine in, 297

E

Eclampsia, renal decapsulation in, 295
Ectopic gestation, ruptured, with free hemorrhage into the abdominal cavity, 147
Edsall, D. L., hygiene of medical cases, particularly in hospital wards, 469
Ellett, E. C., otitis media and its treatment, 105
Emphysema, aspirin in, 763
Empyema, aspiration drainage in treatment of, 64
Endometritis, investigations concerning, 305
Endometrium, changes affecting, 919
Enteric fever, serum therapy in, 454
treatment of, 609
with specific sera filtrates and residues, 453
Enterogenic intoxication, indican reaction as evidence of, 567
Epidemiology of acute poliomyelitis, 647
Epilepsy, treatment of, 912
Epithelioma of vagina, 773
Erlanger, J., irregularities of the heart resulting from disturbed conductivity, 797
Erysipeloid of Rosenbach, 729
Erythema nodosum, etiology of, 621
Estivo-autumnal fever, 612
Eversion of tube in tubal abortion, 307
Exophthalmic goitre, serum treatment of, 453
Extirpation of malignant tumors of tonsillar region, 605
Eyelid, sarcoma of, 300

F

Facial hemiatrophy, 301
neuralgia, treatment of, 449
Femur, fractures of neck of, treatment of, 604
separation of acetabular epiphysis of, 291
Fever, enteric, 453, 454, 609
glandular, acute, 346
miliary, epidemics of, 310
scarlet, 456
Fibroma of ovary, 149
Fibro-myomas, primary, of broad ligaments, 617
Fingers, fractures of, 445
Finney, J. M. T., choice of operation in pyloric stenosis, 333

Fleas, plague of, 466
Fracture of intercarpal joints, 448
Fractures, application of local anesthesia to, 904
of fingers, 445
of neck of femur, treatment of, 604
Freiberg, A. H., the relaxed knee-joint, 696
Fremont-Smith, F., arteriosclerosis in the young, 199
Freyer's operation in cancer of prostate, 135
Fry, H. D., management of labor in minor degrees of pelvic contraction, 704

G

Gall-bladder, congenital absence of, 889
perforation of, during typhoid fever, 541
Gallop rhythm of heart, 670
Gallstones, pathogenesis of, 155
Gangrene, symmetrical, in malaria, 300
Gastric acidity and motility, 753
diseases, alcohol in, 764
bismuth in, 911
mucus, lack of, 207
neuroses, 25
ulcer, Lenhartz treatment of, 18
Gastritis, phlegmonous, 662
Gastro-enterostomy, technique of, 292
Gastro-intestinal infections in typhoid fever, 469
Gastropathies, bismuth subnitrate in, 296
Glandular fever, acute, 346
Granular form of tubercle bacillus unstainable by Ziehl's method, 598
Graves' disease and its treatment, 313
Gunshot wounds of the peripheral nerves, 137

H

Hartford, Connecticut, epidemic cerebrospinal meningitis in, 351
Healing of carcinoma by sunlight, 622
Hearing, impairment of, 309
Heart, action of nitrites on, 99
cases, clinical study of, 790
complications of scarlet fever, 456
gallop rhythm of, 670
irregularities of, 797
surgery of, 447
Hecht, D'Orsay, morbid somnolence, 403
Hematometra, chorio-epithelioma complicated by, 459
Hematuria due to small doses of hexamethylenamine, 142
in pregnancy, 918
Hemiatrophy, facial, 301
Hemoglobinuria, paroxysmal, 622
Hemoglobinuric fever, 910
Hemolytic jaundice, 754
Hemophilia, hemorrhages in, 454
Hemoptysis, treatment of, 140
Hemorrhage, cerebral, during pregnancy, 917
pontile, 408
Hemorrhages, internal, after bilateral castration, 772
Hemorrhagic nephritis, acute, following epidemic parotitis, 768
Hemorrhoids, high-frequency current in, 766
Henry, J. N., purulent cerebrospinal meningitis caused by the typhoid bacillus, without the usual intestinal lesions of typhoid fever, 240
Hepatitis, amœbic, presuppurative stage of, 130
certain unusual forms of, 251
Herniæ, lateral abdominal, 761
Hippus, pathological, 153
Holt, L. E., epidemiology of acute poliomyelitis, 647
Hot-air treatment after abdominal operations, 758
Houghton, H. A., indican reaction as evidence of enterogenic intoxication, 567
Hunter, J. W., Röntgen-ray treatment of hypertrophied prostate, 73
Hydronephrosis, intermittent, 136, 291
Hygiene of medical cases, particularly in hospital wards, 469
Hymen, origin of, 773
Hyperacidity and gastric ulcer, 207
Hyperleukocytosis, nucleinic acid injections in, 143
Hyperplastic changes in mucous membrane of uterus, 307
Hypertrophied prostate, Röntgen-ray treatment of, 73
Hypertrophy of pharyngeal extremities of Eustachian tube, 464
Hypophysis, resection of, 311
Hypospadias, penile, operation for, 145

I

Indican reaction as evidence of enterogenic intoxication, 567
Infancy, Kernig's sign in, 767
Infantile convulsions, treatment of, 296
rectum, prolapse of, 768
Infants, laryngeal papillomas in, 464
nephritis in, 455
Infection, septic, 445
Infections of the biliary passages, 37
Inflammatory diseases of appendages, surgical treatment of, 460
strictures of rectum, 134
Ingraham, C. B., Jr., epidemic cerebrospinal meningitis in Hartford, Connecticut, during 1904–1905, 351
Instrumental perforation of uterus, 618
Intercarpal joints, fracture of, 448

Intermittent hydronephrosis, 136
treated by operation, 291
Interpretation of the positive venous pulse, 284
Intestinal atony, postoperative, physostigmine salicylate in, 297
lesions of typhoid fever, 240
transplantation, formation of an artificial vagina by, 461
Intestine, strangulation of small, 758
Intracranial effusions of blood in newborn, operative treatment of, 614
Intraperitoneal rupture of bladder during labor, 303
Intussusception, acute, in children, 134
Impetigo contagiosa, etiology of, 620
Ionization of silver in treatment of urethritis, 602
Ipecacuanha in amœbic dysentery, 764
Irregularities of the heart resulting from disturbed conductivity, 797

J

Janeway, T. C., use and abuse of digitalis, 781
Jaundice, hemolytic, 754
Joint disease, chronic, tuberculin injections in, 452
Jones, G. I., acute glandular fever, 346
Jopson, J. H., erysipeloid of Rosenbach, 729
Jugular pulse of man, 812
Juxta-balanic penile hypospadias, 760

K

Kauffmann, J., lack of gastric mucus and its relation to hyperacidity and gastric ulcer, 207
Kelly, A. O. J., primary carcinoma and endothelioma of vermiform appendix, 851
Kernig's sign in infancy, 767
Kidney, rupture of, 54
Kidneys, experimental generation of new collateral vessels for, 606
operations on, 625
Knee-joint, relaxed, 696
Koch's old tuberculin in gynecology, diagnostic value of, 150

L

Labia minora, shape of, during menstrual life, 773
Labor, management of, in minor degrees of pelvic contraction, 704
Lambert, S. W., Lenhartz treatment of gastric ulcer, 18
Laparotomy, after-treatment for, 446
Laryngeal complications of typhoid fever, 232
papillomas in infants, 464
tuberculosis, treatment of, 608
Larynx, chronic stenosis of, 575
tuberculous stenosis of, 465
Lateral abdominal herniæ, 761
sinus, rupture of, 445
Lenhartz treatment of gastric ulcer, 18
Ligation of common carotid, 760
Liver, cirrhosis of, tuberculous, 779
diagnosis of affections of, 287
Lowered blood pressure in peritonitis, treatment of, with intravenous adrenalin-saline solution, 136
Lung, gangrene of, 905

M

McBurney's point, 905
McConnell, G., clinical and pathological aspects of rodent ulcer, 719
McMurrich, J. P., congenital adhesions in the common iliac veins, and their relation to thrombosis of the femoral and iliac veins, 342
McWilliams, C. A., primary carcinoma of vermiform appendix, 822
MacKenzie, R., cardiac arrhythmia due to extra systoles originating in the bundle of His, 534
MacNider, W. de B., action of nitrites on the heart, 99
Magnesium salts, action of, on the peripheral motor nervous system, 624
physiological and pharmacological studies of, 154
Malaria in children, 295
Malignant tumors of tonsillar region, extirpation of, 605
Malnutrition in older children, 613
Management of labor in minor degrees of pelvic contraction, 704
Mastoid operation, radical, 445
Measles and rubeola, 298
Measuring the venous pressure without a manometer, 285
Mechanical obstruction by torsion of the whole of the small intestine and its mesentery, 444
Mediastinum, carcinoma of, 529
Medical cases, hygiene of, 469
Meningitis, bacteriology of, 613
Menstruation, precocious, 612
Mental diseases, potassium iodide in, 765
Mercury bibromide in syphilis, 608
Metallic resonance, 597
Method of introducing air into the mouth of a child born in breech presentation, 770
Microbic cyanosis, observations on, 442
Migraine, ophthalmoplegic, 776
Miliary fever, epidemics of, 310
Modified milk, caloric value of, 767
Moebius' antithyreoidin, specific action of, 611
Morbid somnolence, 403
Morphine in cardiac dyspnœa, 297

Morrow, W. S., cardiac arrhythmia due to extra-systoles originating in the bundle of His, 534
Mucous membrane of uterus, hyperplastic changes in, 307
Multiple telangiectases, 443
Muscular connection between the auricle and the ventricle in normal hearts and in Adams-Stokes disease, 155
Myocarditis, fibrous, chronic, 244
Myopia, treatment of, 152
Myxœdema, 132

N

Nasal cough, 465
tuberculosis, primary, 464
Neilson, T. R., rupture of the kidney, with remarks upon conservative operative treatment, 54
Nephritic œdema, 128
Nephritis in infants, 455
late secondary, 289
toxic, 127
Nephrotomy, transverse incision for, 446
Nervous diseases, functional, treatment of, 168
manifestations of arteriosclerosis, 187
system, syphilitic lesions of, 551
Neuralgia, facial, treatment of, 449
Neurasthenia in the young, treatment of, 178
of auto-intoxication, 558
New flap operation for vesicovaginal fistula, 773
Nitrites, action of, on heart, 99
Nocturnal petit mal, 94
Noma, bacteriological findings in, 769
Novocain as a lumbar spinal anesthetic, 290
Nucleinic acid injections in the induction of hyperleukocytosis, 143
Nystagmus, unilateral mixed, 269

O

Obesity, treatment of, 139
Occurrence of congenital adhesions in the common iliac veins, 342
Ochronosis, 755
Œdema, nephritic, 128
Œsophagus, foreign body in, mistaken for carcinoma, 463
Ophthalmic reaction in diagnosis of typhoid fever, 751
to tuberculin, 599
Ophthalmoplegic migraine, 776
Ophthalmo-tuberculin diagnostic test, 440
Opsonic treatment of tuberculosis by tuberculin, 610
Orbison, T. J., neurasthenia of auto-intoxication, 558
Osborne, O. T., nature and the management of diabetes mellitus, 508
Osteomalacia, parathyroid glands in, 903
treated by section at term, 917
Otitis media, acute, so-called cyclic course of, 308
treatment of, 105
by method of induced hyperemia of Bier, 308
Otogenous thrombosis of bulb of internal jugular vein, 762
Outdoor air treatment of pneumonia, 13
Ovarian cyst, rupture of, during pregnancy causing grave internal hemorrhage, 149
hematoma, 919
tumors, 920
Ovary and tube and ovarian tumors in inguinal canal, 307
carcinoma of, 150
fibroma of, 149
papilloma of, 921
prolapse of, treatment of, 306
sarcoma of, during pregnancy, 460
sarcomatous cyst of, 151
tumors of, 305
Oxyuris vermicularis, 290
Ozena, 464

P

Paget's disease treated by *x*-rays, 622
Palsy, congenital, of oculomotor nerve with continuous movements of pupil, 776
Pancreas, tumors of head of, 135
Paralysis of accomodation in diabetes, 776
of recurrent nerve in tuberculosis, 464
of sixth pair of cranial nerves after rachistovainization, 777
Parametritis, purulent, operative treatment of, 619
Parathyroid gland, function of, 779
Parietal bone, depression of, in a newly born infant relieved by trephining, 457
Parovarian tumor, an unusual, 619
Parovarium, sarcoma of, 149
Paroxysmal hemoglobinuria, 622
Pelliculous sore throat, 463
Pelvic floor, anatomy of, 916
infections, treatment of, 618
viscera, supports of, 774
Penile hypospadias, operation for, 145
Penis, human, bone formation of, 293
Percussion in diagnosis of respiratory disease, 439
Perforation of gall-bladder during typhoid fever, 541
Peri-arteritis nodosa, 623
Pericolitis sinistra, 758

Peripheral motor nervous system, action of magnesium salts on, 624
nerves, gunshot wounds of, 137
Perkins, J., carcinoma of the mediastinum, simulating aneurysm, 529
Pernicious anemia, pathogenesis of, 285
Peroxide of hydrogen in diseases of ear, nose, and throat, 924
Petit mal, nocturnal, 94
Pharyngeal diphtheria, 145
Pharynx, tumors of, 464
Phlebitis following abdominal operations, 620
Phlegmonous gastritis, 662
Physostigmine salicylate in prevention of postoperative intestinal atony, 297
Piersol, G. M., observation on jugular pulse of man, 812
Plague of fleas, 466
Pleurisy, treatment of, 911
Pneumonia, colloidal metals in, 451
epidemic, 440
outdoor-air treatment of, 13
Poliomyelitis, epidemiology of acute, 647
Polyarteritis acute nodosa, 623
Polyvalent antidysenteric serum, 454
Pontile hemorrhage, 408
Portugal, blindness in, 153
Potassium iodide in mental diseases, 765
Potatoes in diabetes, 763
Precocious menstruation, 612
Presuppurative stage of amœbic hepatitis, 130
Primary carcinoma of vermiform appendix, 702, 822, 851
Primitive renal lithiasis, 449
Progressive muscular dystrophy, 244
Prolapse of infantile rectum, 768
of ovary, treatment of, 306
Prolapsus uteri, abdominal colpopexy for, 151
end results in operations for, 619
Prostatic cancer removed by the operation of Freyer, 135
Pruritus vulvæ, treatment of, 911
Pseudoherniæ, 761
Pseudoptosis with hysterical amblyopia following injury, 777
Psychasthenia, treatment of, from the standpoint of the social consciousness, 77
Psychotherapy, 168
Pubiotomy in America, 771
Röntgen-ray examination after, 616
Pulmonary tuberculosis and induced abortion, 283
Pulse and blood-pressure changes in aortic insufficiency, 752
Pulse, jugular, of man, 812
Purpura, treatment of hemorrhages in, 454
Purulent cerebrospinal meningitis caused by the typhoid bacillus, 240
Putnam, J. J., treatment of psychasthenia from the standpoint of the social consciousness, 77
Pyroligneous acid in arthritis deformans, 141
Pyloric stenosis, choice of operation, 333

R

Racemose arterial angioma, 907
Radical mastoid operation, 444
Raw *vs.* sterilized milk, 926
Reaction of phagocytes of elephant's blood on the bacilli of tuberculosis, 584
Rectal feeding, gastric secretion in, 900
Rectum, strictures of, 134
Reflexes in scarlet fever, 756
Relaxed knee-joint, 696
Renal catheter as an aid in diagnosis of valve-like obstruction of ureter, 618
decapsulation in eclampsia, 295
lithiasis, primitive, 449
Resonance, metallic, 597
Respiratory disease, percussion in diagnosis of, 439
Retroversion and retroflexion of the pregnant uterus, 147
Reviews—
Abel, Handbook of Bacteriology, 897
Allbutt, System of Medicine, 590
Babcock, Diseases of Lungs, 435
Ballantyne, Green's Encyclopedia and Dictionary of Medicine and Surgery, 750
Barwell, Diseases of Larynx, 747
Bruce, Materia Medica and Therapeutics, 427
Bryant, American Practice of Surgery, 280, 430
Church, Modern Clinical Medicine, 892
Corner, Operations of General Practice, 897
Crossen, Diagnosis and Treatment of Diseases of Women, 277
DeGarmo, Abdominal Hernia, 741
Egbert, Manual of Hygiene and Sanitation, 595
Forel, Hygiene of Nerves and Mind in Health and Disease, 278
Fowler, Operating Room and the Patient, 898
Ghosh, Treatise on Materia Medica and Therapeutics, 427
Hardaway, Handbook of Cutaneous Therapeutics, 592

Reviews—
Hare, Progressive Medicine, 434, 744
Text-book of Practical Therapeutics, 122
Text-book of Practical Diagnosis, 122
Jacobson and Rowlands, Operations of Surgery, 587
Jewett, Practice of Obstetrics by American Authors, 277
Kassabian, Electrotherapeutics and Röntgen Rays, 744
Keogh, Manual of Venereal Diseases, 896
Laveran, Trypanosomes and Trypanosomiasis, 743
Lewis, Stöhr's Histology, 123
Longcope, International Clinics, 746
Manson, Tropical Diseases, 749
May, Manual of the Diseases of the Eye, 438
McIsaac, Primary Nursing Technique for First-year Nurses, 126
McVail, Prevention of Infectious Disease, 895
Morat, Physiology of the Nervous System, 117
Morris, Light and *X*-ray Treatment of Skin Diseases, 740
Nothnagel, Diseases of the Intestines and Peritoneum, 126
Osler, La Pratique de la Médecine, 596
Osler, Modern Medicine, Vol. II, 275
Park, Principles and Practice of Modern Surgery, 113
Piersol, Human Anatomy, 271
Reissig, The Standard Family Physician, 119
Rodman, Diseases of Breast, 891
Schlief, Materia Medica, Therapeutics, Pharmacology, and Pharmacognosy, 427
Shoemaker, Practical Treatise on Materia Medica and Therapeutics, 427
Sobotta, Atlas and Text-book of Human Anatomy, 439, 749
Sollman, Text-book of Pharmacology, 427
Stephenson, Ophthalmia Neonatorum, 279
Stewart, Manual of Surgery, 596
Stimson, Fractures and Dislocations, 748
Tod, Diseases of the Ear, 747
Turner, Epilepsy, 593
Waggett, Diseases of the Nose, 747
Wallace, Prostatic Enlargement, 124
Williams, Obstetrics, 894
Wood, The Commoner Diseases of the Eye, 437
Wylie, Foods and their Adulteration, 436
Yeo, Manual of Medical Treatment or Clinical Therapeutics, 427
Revolver ball tolerated for six years, 138
Rieser, W., laryngeal complications of typhoid fever, 232
Robinson, G. C., gallop rhythm of the heart, 670
Rodent ulcer, clinical and pathological aspects of, 719
Rogers, J., treatment of chronic stenosis of the larynx and trachea, 575
Röntgen-ray, abortion produced by, 617
examination after pubiotomy, 616
in sarcoma, 766, 912
treatment of hypertrophied prostate, 73
of syringomyelia, 288
Rosenbach, erysipeloid of, 729
Rosenberger, R. S., purulent cerebrospinal meningitis caused by the typhoid bacillus, without the usual intestinal lesions of typhoid fever, 240
Rötheln, arthropathy in, 146
Rupture of bladder, 303
of cervix in abortion, 772
of kidney, 54
of lateral sinuses, 445
Russ, R., surgical aspects of Dupuytren's contraction, 856

S

Santonin in diabetes, 609
Sarcoma of eyelid, 300
of ovary during pregnancy, 460
of parovarium, 149
Röntgen-rays in, 766
Sarcomatous cyst of ovary in an hermaphrodite having a masculine appearance, 151
Scarlet fever, certain reflexes in, 756
heart complications of, 456
Schley, W. S., aspiration drainage in the treatment of empyema, 64
Scopolamine-morphine anesthesia during labor, 770
Seasickness, veronal in, 298
Selby, C. D., complications and sequels of typhoid fever, 224
Semicircular canals, disturbance of equilibrium resulting from diseases of, 310
Septic infection, 445
Serum, antidiphtheritic, in general therapeutics, 453
therapy in enteric fever, 454
treatment of exophthalmic goitre, 453
Sewage bacteria in air, 468

Sigmoid flexure, simple inflammatory affections of, 602
Sigmoiditis and perisigmoiditis, 602
Skin diseases, carbolic acid in, 621
vaccine treatment in, 608
reactions to tuberculin, 599
Sodium anilarsenate in syphilis, 140
bibromomercurate in syphilis, 454
cacodylate, 763
Somnolence, morbid, 403
Sore throat in epidemic cerebrospinal meningitis, practical importance of, 299
pelliculous, 463
Specific immunity and *x*-ray therapeutics, 420
sera filtrates and residues in treatment of enteric fever, 453
Spiller, W. G., tumors of the cauda equina and lower vertebræ, 365
Spinal anesthesia, 133
Spleen, diagnosis of, affections of, 287
Splenectomy for carcinoma, 603
in Banti's disease, 604
Stab wound of fœtus in utero, 918
Steiner, W. R., epidemic cerebrospinal meningitis in Hartford, Connecticut, during 1904–1905, 351
Stengel, A., nervous manifestations of arteriosclerosis, 187
Stenosis, chronic, of larynx, 575
Stock vaccines *vs.* autogenous vaccines in therapeutics, 765
Stone, I. S., congenital absence of gall-bladder, 889
Strangulation of small intestine through a rent in the mesentery, 758
Streptococci, relation of, to thrombosis, 302
Strictures of rectum, 134
Strychnine, harmlessness of large doses of, 140
Stuttering, 465
Suppurative inflammation, acute, treatment of, by passive congestion, 447
phlegmonous gastritis, 662
Surgery of heart, 447
Symmers, D., certain unusual forms of hepatitis, 251
Symmetrical gangrene occurring in patients with malaria, 300
Syphilis, alterations in umbilical cord produced by, 457
mercury bibromide in, 608
sodium anilarsenate in, 140
bibromomercurate in, 454
treatment of, 139
Syphilitic lesions of nervous system, 551
Syringomyelia, Röntgen-ray treatment of, 288

T

Telangiectasis, multiple, 443
Testicle, diseases of, in children, 299
Thompson, W. G., treatment of pneumonia, especially by outdoor air, 13
W. H., Graves' disease and its treatment, 313
Thrombosis of bulb of internal jugular vein, 762
of femoral and iliac veins, 342
Thyroid gland, function of, 779
Tileston, W., primary tumors of adrenal gland in children, 871
Tobacco smoke, action of, upon blood-vessels of rabbits, 312
Torsion of appendices epiploicæ, 864
Toxemia during pregnancy, 917
from the standpoint of perverted metabolism, 688
Toxic nephritis, 127
Trachea, chronic stenosis of, 575
Transfusion of blood from vena cava to portal vein by means of a termino-lateral anastomosis, 906
Transplantation, bone, 290
Transverse incision for nephrotomy, 446
lesion of spinal cord, symptom complex of, 735
Trichomonas hominis intestinalis, 752
Trichophytosis, special form of, as a sequel of the permanent bath, 621
Tricocephaliasis, 144
Trypanosome infection through the mucous membrane of gastro-intestinal tract, 311
Trypanosomiasis, sodium anilarsenate in, 910
Tubal abortion, eversion of tube in, 307
Tuberculin injections in chronic joint disease, 452
skin, and ophthalmic reactions to, 599
Tuberculosis, bacilli of, 584
diagnosis of, 900, 901
laryngeal, treatment of, 608
nasal, 464
of alimentary orifice, 924
of neck of uterus, 775
opsonic treatment of, by tuberculin, 610
paralysis of recurrent nerve in, 464
pulmonary, and induced abortion, 283
Tuberculotherapy in tuberculosis, 610
Tuberculous cirrhosis of liver, 779
elbow joints, 908
stenosis of larynx, 465
Tumor, parovarian, 619
Tumors, abdominal, diagnosis of, 605
malignant, trypsin in, 910
of adrenal gland, 871
of cauda equina and lower vertebræ, 365

Tumors of head of pancreas, 135
of ovary, 305
of pharynx, 464
Typhoid carriers, 468
fever, 224, 240
gastro-intestinal infections in, 469
laryngeal complications of, 232
ophthalmic reaction in diagnosis of, 751
perforation of gall-bladder during, 541
Tyson, J., diagnosis and treatment of cardiovascular-renal disease, 1

U

Ulcer, gastric, 207
of stomach, 899
rodent, 719
Ulcus serpens, practical experience with serum therapy in, 152
Umbilical cord, alterations in, produced by syphilis, 457
Unilateral mixed nystagmus, 269
Uniting a double uterus, 150
Ureter, obstruction of, 618
Ureters, operations on, 625
Urethra, origin of, 773
Urethritis, treatment of, by ionization of silver, 602
Urine testing, danger in, 130
Use and abuse of digitalis, 781
Uterine myomas, parasitic, 921
Uterus, carcinoma of, 774
chorio-epithelioma of, 412
complete extrusion of, 149
four years after Cesarean section, 304
hyperplastic changes in mucous membrane of, 307
instrumental perforation of, 618
tuberculosis of neck of, 775
uniting a double, 150

V

Vaccine therapy in bacterial diseases, 765
Vaccine treatment in skin diseases, 608
Vaccines, bacterial, 451
Vagina, origin of, 773
primary epithelioma of, 773
Valve-like obstruction of ureter, renal catheter as an aid in diagnosis of, 618
Vasodilators in cardiac disease, 607
Veasey, C. A., unilateral mixed nystagmus, 269
Venous congestion, compensatory, 441
pulse, positive, interpretations of, 284
Ventral fixation of round ligaments, 619
Vermiform appendix, carcinoma of, 702, 822, 851
Veronal in seasickness, 298
Vertigo of Ménière, diagnosis of, 922
Vesicovaginal fistula, cystoscope findings in, 461
new flap operation for, 773
Virchow's leontiasis ossea, 907
Viscera, pelvic, supports of, 774
Vulva, carcinoma of, 775

W

Webster, R. W., toxemia from the standpoint of perverted metabolism, 688
Weisenburg, T. H., diagnosis and treatment of syphilitic lesions of the nervous system, 551
White, E. H., primary colloid carcinoma of the vermiform appendix, 702
Willson, R. N., pathogenesis and treatment of neurasthenia in the young, 178
Wolbach, S. B., primary tumors of adrenal gland in children, 871

X

X-ray therapeutics, 420
X-rays, Paget's disease treated by, 622